Using deep neural networks to determine the impact of high-frequency oscillations in epileptic pediatric patients

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Abstract

Worldwide, around 50 million people suffer from epilepsy, making it one of the most common neurological disorders. Children with epilepsy are one group that is particularly at risk because their brains have not fully matured yet. However, there are relatively few studies in the literature on the impact of age on epilepsy and its effects on pediatric patients. More research must be done to understand the neural activity of children with epilepsy and how it changes across children of various ages. In addition, the complex data sets that are generated from existing studies lack a robust and reliable pipeline to analyze high-dimensional electroencephalography. In this study, we elucidate how the scalp topography of HFOs changes with age and how spectral frequency influences these topographies by using a convolutional neural network (CNN) autoencoder for unsupervised clustering of the topographies. We accomplish this goal by investigating a publicly available data set on the OpenNeuro platform containing EEG data and information about high-frequency oscillations (HFOs) in youth. Our study confirms that HFOs change with age and spectral frequency. Furthermore, we provide a reliable and powerful pipeline to process high-dimensional medical data through our usage of a CNN autoencoder. This research is an important step in assessing HFOs as a biomarker in pediatric epilepsy detection and treatment.

Keywords: epilepsy, convolutional neural networks, pediatrics, high-frequency oscillations, autoencoder

Introduction

Epilepsy is a neurological disorder that causes patients to get anywhere from less than one seizure per year to several per day [1]. Approximately 1% of the world's population suffers from epilepsy, and 75% of cases of epilepsy begin in childhood [2-3].

Children, because of their underdeveloped brains, face elevated risks, experiencing detrimental interictal spikes between seizures. These spikes, brief periods of abnormal electrical activity, have long-term negative effects on developing neural circuits, including irreversible brain damage, cell loss, and loss of neural connectivity [3]. These issues often lead to substantial deficits concerning learning and memory, as well as a variety of co-morbidities. [4]. They also increase children's risk for seizure-related injuries in later stages of life.

Given the severity of the problem, identifying reliable biomarkers to understand and diagnose epilepsy is crucial. High-frequency oscillations (HFOs) have risen in popularity among researchers as biomarkers [5]. HFOs are aberrant electrical signals in the brain that are observed in intracranial and scalp electroencephalography scans. They are commonly divided into two spectral frequency bands: ripples (80-250 Hz) and fast ripples (>250 Hz) - although the exact definitions of these ranges vary across different studies [6]. To obtain fast ripples, extremely high sampling frequencies are needed, leading to significant storage, processing, and computation time requirements [7]. Thus, we decided to focus on ripples.

Research indicates that the spectral frequency of HFOs decreases with age [8]. However, there is little research on how the location of HFOs in the brain changes with age. Additionally, previous research states that the technological and methodological requirements for EEG analysis must be defined and reliable [9]. There is currently no formal pipeline for EEG analysis and extracting information from high-dimensional medical data. Because pediatric epilepsy is so hard to detect, we must find more reliable ways to detect it more easily in clinical settings [10]. With more research on this, we provide information that improves the reliability of HFOs as biomarkers for pediatric epilepsy.

In this paper, we look into the location of HFOs within the ripple band and the brain topography of epileptic pediatric patients. We examine how these change with age. We hypothesize that the brain topography of younger children would contain more abnormalities, as they have higher HFOs. We also analyze specific spectral frequency bands within the ripple band and their impact on children's brain topography. As epilepsy severity increases, higher rates of HFOs can be observed [11]. Thus, we predict that higher spectral frequency bands would have more impact on brain topography.

Our research determines a reliable pipeline to extract information from high-dimensional medical data. We found variations in HFO location and spectral power amongst different age groups. We also identified specific areas where more data is needed for future studies. By providing more information about HFOs in children's brains, we help the field move one step closer to using HFOs as a reliable and cost-effective biomarker to detect pediatric epilepsy in a clinical setting.

Methods

Data

The data used in this project was obtained from a study conducted by Dorottya Cserpán et al., which can be found on the OpenNeuro platform [6]. In this experiment, researchers took scalp EEG readings at 3-hour intervals from 30 pediatric epileptic patients (ages 0.7 to 17.4 years) undergoing non-rapid eye movement (NREM) sleep. The configuration used was the international 10-20 electrode placement system and the sampling frequency was 1024 Hz. There were 16 female and 14 male patients, each with focal or generalized epilepsy. Focal epilepsy is a form of epilepsy that affects a specific region of the brain, while generalized epilepsy affects both hemispheres of the brain and usually starts in childhood [12]. In this dataset, 9 patients had generalized epilepsy, while the other 21 had focal.

Modeling

To select the most useful features in the raw EEG data, we carried out several preprocessing steps. We used the MNE library to carry out most of these steps [13]. Since the highest frequency for ripple HFOs is 250 Hz, we resampled each EEG scan to twice this rate, yielding a sampling rate of 500 Hz. After this, we applied bandpass filters to the data within the ripple rate frequencies. We created a total of 17 bands per subject, each with a range of 10 Hz (80-90 Hz, 90-100 Hz, etc.). Then, we visualized the topography of each patient at each frequency band at various time windows. Each subject had 18 time windows (except subject 19, which had 12 time windows), each 10 minutes long. This ultimately yielded 306 topographies per subject. Each subject's topography images were then saved as a single TensorFlow tensor of shape $[18_{\text{\#of time windows}} \times 125_{\text{\#of vertical pixels}} \times 125_{\text{\#of horizontal pixels}} \times 17_{\text{\#of frequency bands}}]$. Finally, we used pixel normalization to scale the values of the pixels from 0 to 1.

To reduce the data size that we pass into a KMeans algorithm, we constructed an autoencoder. The autoencoder is trained to reconstruct each image and is comprised of three modules: an encoder, a bottleneck, and a decoder. The size of the latent space in the bottleneck was 10, which was found after letting the latent space be a hyperparameter and tuning it. We tried various latent space sizes, setting the latent space as low as 5 and as high as 1000. We found that a size of 10 allowed the model to reach a low loss with a small latent space size. The architecture of the autoencoder is shown in Figure 1.

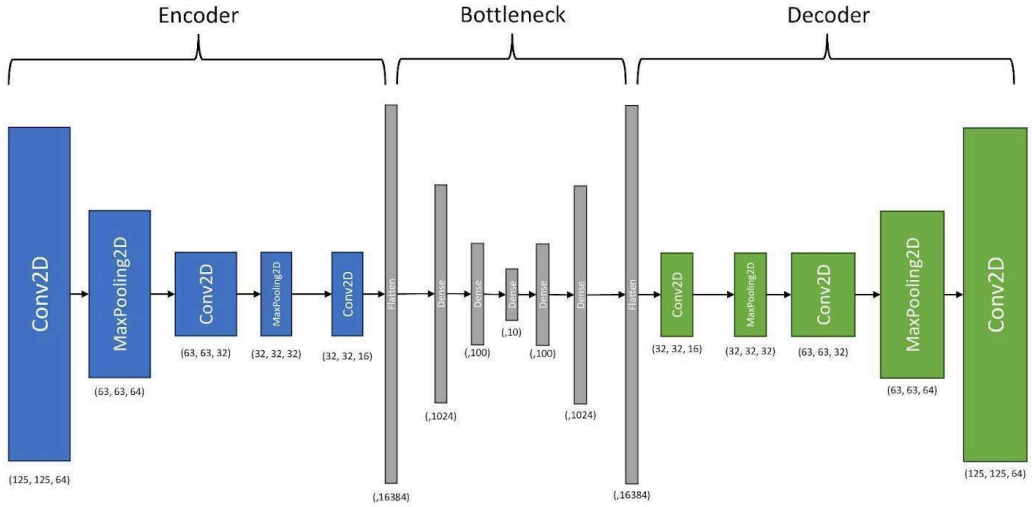

Figure 1. The architecture of the autoencoder. The autoencoder included an encoder, bottleneck, and decoder. Both the encoder and decoder have 5 layers, and the bottleneck of the autoencoder reduces the data to a latent space of (1,10). We used TensorFlow's Convolutional 2D, MaxPooling 2D, Flatten, and Dense layers to build the autoencoder.

The autoencoder was trained for 100 epochs on the normalized data.

We applied a mask on the images before using the mean-squared error loss function to ensure that we only trained on the topographies and not the white backgrounds of each image. The custom loss function applied a mask on the white pixels and computed the mean squared error of the non-white pixels. By doing this, we made sure that our autoencoder was training and learning the most important parts of the image. This technique yielded more accurate reconstructions, and thus latent representations, of the data, as seen in Figure 2. The reconstructions were very similar to the original image, confirming that the autoencoder was able to learn a sufficient amount about the data and reconstruct it accurately. The model's loss of 0.0029 showed us that it was able to fit the data well.

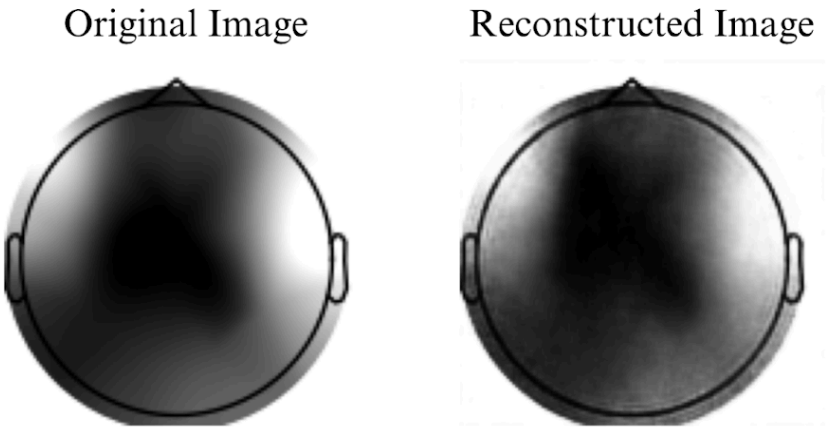

Figure 2. On the left of Figure 2 is the original image that we were attempting to reconstruct, and the right shows our autoencoder's reconstructed image. The reconstructed image was very similar to the original image but was more pixelated.

After training our model, we used the encoder part of the model to yield a tensor of size (535, 10), which contained each sample's latent representation.

Finally, the encoded representation was passed into a KMeans algorithm to discern three clusters from the data. We let the number of clusters be a hyperparameter and tuned it accordingly, ultimately deciding that three clusters were the optimal number.

Analysis

Our threshold for our model's loss was 0.05. This is a low enough loss that we felt comfortable with the accuracy of our autoencoder. We set our threshold based on previous autoencoder studies, most of which used a loss of .03 to .10.

To answer our research questions and analyze the data, we decided to employ two main analysis methods: a correlation test and a visual inspection of the topographies. We performed a correlation test to attempt to discover the relationship between the variability in HFO spectral power over age. Visual inspection of the topographies allows us to understand the spatial impact of HFOs in the brain.

Results

Autoencoder

Figure 3 displays the loss over epochs of the autoencoder, which converged to a loss of 0.0029. The autoencoder's activation function was Leaky ReLu, which ensured that the model converged more accurately and faster. Batch Normalization layers were also utilized, which decreased the loss from 0.0703 to 0.0029 (reducing it by a factor of almost 25).

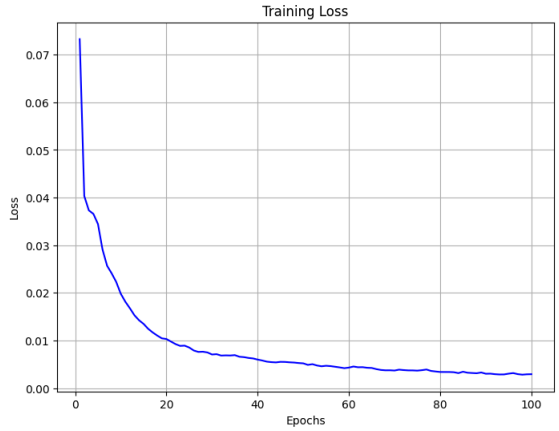

Figure 3. The loss of our model decreased to 0.0029 after training for 100 epochs with a batch size of 32.

Clustering

The three clusters yielded from KMeans had 104, 218, and 213 patients respectively. Figures 4 and 5 show a t-SNE visualization of the three clusters, along with a visualization of each patient's data points. These figures show that cluster 1 has more older subjects than any other cluster. However, other than this, the visualization doesn't seem to display much correlation between age and the clusters. KMeans was also unable to cluster based on focal vs. generalized epilepsy, as seen in Figure 6.

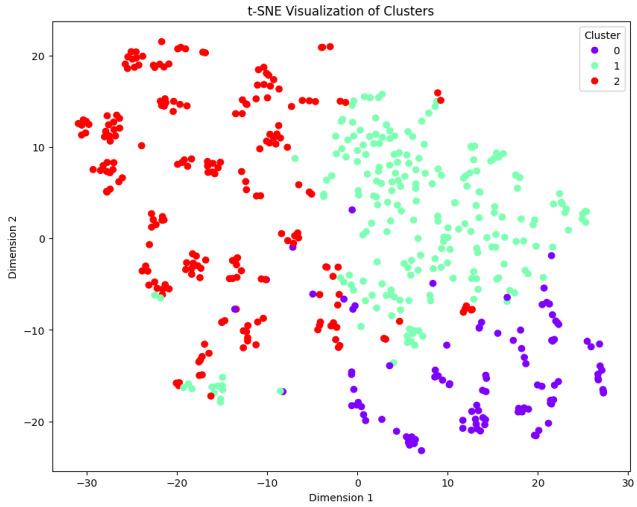

Figure 4. The t-SNE algorithm was used to visualize the 3 clusters in a 2D space.

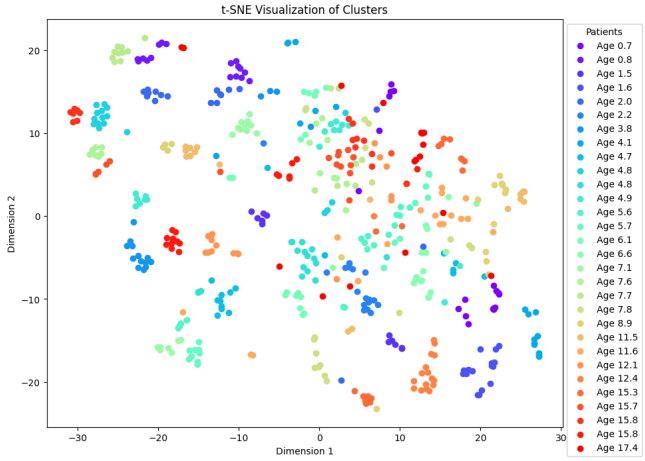

Figure 5. The t-SNE algorithm was used to visualize each patient's data in a 2D space and colored their markers by age to understand the correlation between KMeans clustering and age.

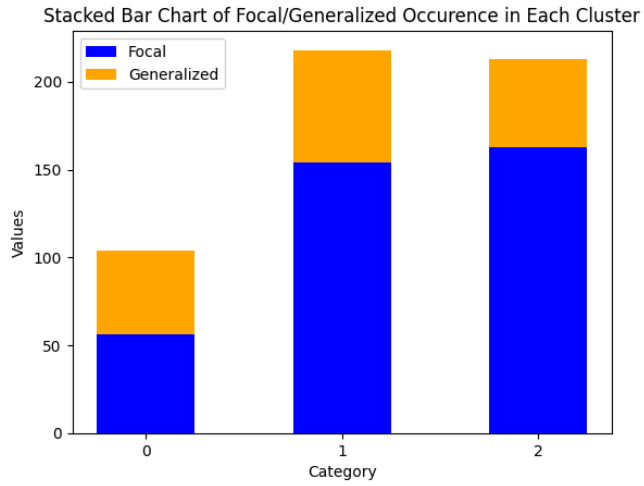

Figure 6. This visualization shows the distribution of focal and generalized epilepsy in each cluster, displaying an even distribution of focal and generalized epilepsy in each cluster.

Figure 7 displays the topography of each frequency in each cluster's central data point. The darker regions depict a lower power spectral density (PSD), whereas the lighter regions of each topography depict a higher PSD. The regions with high PSD are the regions where an epileptic HFO occurred in the patient. Figure 7 indicates that cluster 0 tends to exhibit HFOs in the front of the brain, with lower frequencies (especially those in the 80-100 Hz range) exhibiting more HFOs than higher frequencies. This cluster also seemed to decrease with age, as displayed in Figure 8.

Figure 7. We plotted the topography of each frequency at each cluster's central data point to understand the differences in topographies among the various frequencies.

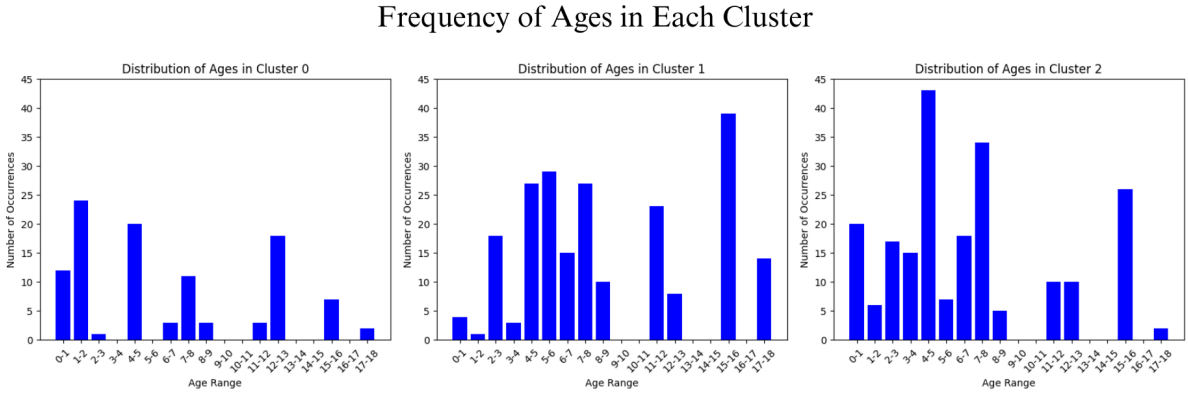

Figure 8. We plotted the number of occurrences that a patient in each age range appeared in every cluster.

Cluster 1 was the most prevalent in the age range of 4-8, with a large peak at 15-16 years, as indicated by Figure 8. This cluster increased with age. HFOs were consistent across all frequency ranges.

According to Figure 8, cluster 2 was most prevalent in younger patients, with a peak at 4-5 years. As indicated by Figure 7, the central data point showed that patients exhibited HFOs occurring in various locations in the brain, depending on the frequency. Generally, the HFOs seemed to occur in the back of the brain. However, the HFOs at higher frequencies, 240-250 Hertz, were quite different from those at different brain frequencies.

Variability in the HFO Spectral Power

Figure 9 depicts each patient's data points' standard deviation as a function of age. Essentially, it shows the variability in each patient's HFOs' spectral power. From the figure, it can be seen that the variability decreases with age. However, there was no significant correlation between HFO location and spectral power variability, and age ($r = -.24,\ p = .19$).

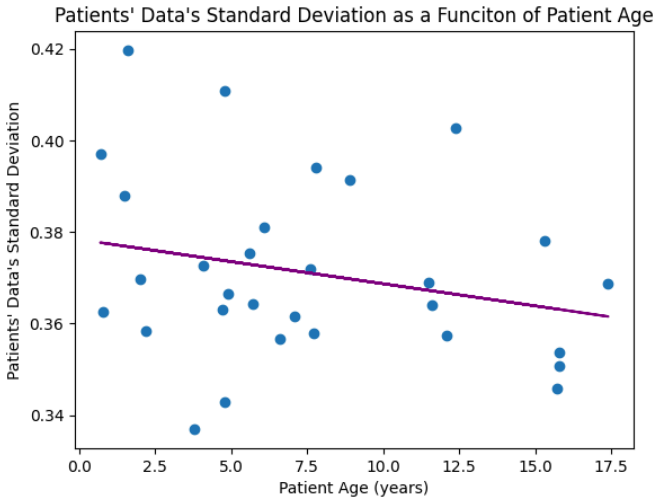

Figure 9. This visualization shows the correlation between patients' age and the standard deviation between the topographies of each spectral frequency, which represents the variability in each patient's HFOs' spectral power.

Discussion

Our paper is one of the first papers to use an autoencoder to examine the impacts of age on high-frequency oscillations in epileptic youth. We find evidence that HFOs change with age and spectral frequency. Older patients tended to have HFOs at different brain locations and frequencies. As age increased, the presence of HFOs in the front of the brain decreased. Additionally, our data showed no significant correlation between variability in HFO spectral power and age, which is in line with previous literature [14].

Autoencoder

Our convolutional neural network (CNN) autoencoder proved to be a valuable way to analyze the correlation between EEG recordings and brain topographies. Although there are ways to improve the autoencoder, which we discuss later, we recommend this general pipeline to future researchers examining this field, as it is an accurate and reliable way to visualize and analyze brain topographies based on EEG data.

Passing in a condensed representation of our data is crucial to this dataset. People with epilepsy have large variability in the spatial, temporal, and spectral frequency domains. This means that there was a lot of noise in our dataset. Our CNN autoencoder is critical because it allows for a transformation of the input images to a reduced dimensionality, which allows us to denoise our dataset. By transforming the input images, we passed in a condensed representation of our data to KMeans, ensuring that only the most important information was used for clustering and that irrelevant information was eliminated. By using an autoencoder, we were able to extract the most important features of the data and represent it in a much more condensed, but still accurate, way.

This technique of using a CNN autoencoder to extract features of high-dimensional data is powerful. By only applying KMeans to the most important features of the data, we were able to get rid of noise and represent it more accurately. The pipeline used in this paper can be applied

in many other medical imaging problems to ensure accuracy and efficiency, even if there are not large quantities of data available.

Impact of Age on the Location of HFOs

Our research indicated that younger patients tend to exhibit different HFO activity in lower frequencies. They had higher spectral power and more HFO activity in lower frequencies. On the other hand, HFO activity was much more consistent in their spatial localization in older patients. This finding is in line with previous literature showing that epilepsy in children stabilizes as they grow older [15].

Focal vs. Generalized Epilepsy

Our model was unable to create clusters based on whether the patients had generalized vs. focal epilepsy. This is likely because we performed unsupervised learning on the data. If the data was labeled and supervised clustering was used, better separation along these labels would be expected. Furthermore, because our autoencoder was fairly shallow, with only 5 layers in the encoder and decoder respectively, it may not have been able to learn very complex patterns within the data. Making the autoencoder deeper would ensure that it can solve more specific problems.

Additionally, experimenting with different latent space sizes would likely yield different results. The authors of this paper attempted various latent space sizes between 5 to 100. However, there is a possibility that the latent space that we ultimately chose, 10, is not able to represent all of the complexities of that data.

Current Limitations

There are very few freely accessible online datasets that include pediatric patients' brain topographies while undergoing epileptic shocks. The dataset from Dorottya Cserpán et al. was one of the better choices. However, this dataset was quite small and only included 30 patients, which limits the statistical power of any inferences drawn.

The preprocessing and autoencoder itself had a few limitations. Most significantly, one single autoencoder cannot be used on such a diverse group of patients. Each patient has many variations in how epilepsy manifests itself, so a single autoencoder cannot train itself to recognize all of these differences. Additionally, we decided to use a CNN autoencoder, as we wanted to examine the brain topographies of epileptic youth. However, it is possible that the EEG data would be better represented in alternative forms, such as looking at the raw time amplitude series EEG data. This may yield a better way to model the data.

Furthermore, EEG data may not be the best way to find accurate topographies. Neuroimaging techniques like magnetic resonance imaging (MRI) and functional magnetic resonance imaging (fMRI) are considered to be more accurate ways to understand the topography of the brain. Research that uses different neuroimaging techniques may yield results that are more representative of what is happening in the brain.

Future Directions

Considering the lack of publicly available datasets in the field of pediatric epilepsy and HFO detection, the scientific community must work together to release this type of data online. Furthermore, we plan to research the impact of age on HFO spectral power. Literature [15] shows that children are at substantially higher risk for epilepsy than young adults. We hypothesize that HFO spectral power would decrease as children grow older; however, due to the size of our dataset, we were not able to find a significant correlation. After we obtain a bigger and more robust dataset, we may find a correlation. Finally, this paper provides evidence that HFOs change with age. We plan to extend our findings by researching why and how HFOs change with age.

One direction that we are interested in exploring is modeling the data differently by trying deeper architectures for the autoencoder. This will ensure that the autoencoders' resultant latent spaces will capture all of the variability and unique features of the patients.

We also plan to use raw time-amplitude series EEG data to model the data. A recurrent neural network (RNN), specifically a long short-term memory (LSTM), may be able to capture the patterns in the EEG data better, as they are designed for time series analysis. RNNs are very good at detecting complex patterns in time series data. They have been used for EEG data in the past, and have yielded promising results in similar fields [16]. By attempting to model this data with an RNN, we may be able to find patterns that a CNN could not detect otherwise. Utilizing a CNN allowed us to understand the influence of HFOs on spatial data, which helped us understand the impact of HFOs on topographies. With an RNN, on the other hand, we could delve deeper into the patterns in the spectral frequency of HFOs across time.

Furthermore, time-series transformers have been used in similar domains in the past. A study by Katrompas et. al shows that transformers tend to show superior performance to RNNs or CNNs, making this a promising modeling architecture for us to explore in the future [17].

This study provides a critical insight into the ways that HFOs manifest in the brains of pediatric epileptic patients, moving the field one step closer to using HFOs as biomarkers in clinical settings. With further research on their specific impacts on the brain, HFOs can prove to provide valuable insights into future diagnosis and treatment methods.

Conclusion

Our research delves into the complex landscape of pediatric epilepsy, with a specific focus on the correlation between age, high-frequency oscillations, and brain topography. Using an online dataset containing EEG data of 30 epileptic youth patients while undergoing NREM sleep, we developed a convolutional neural network autoencoder and KMeans clustering, to discern patterns within the data. Our findings shed light on age-related variations in HFO patterns, particularly how different age groups contain variations in HFO location and spectral power. We also provide a general pipeline for future researchers to use while dealing with high-dimensional medical data. In the future, we plan to explore different model architectures, like RNNs and transformers, to model the data more accurately. By addressing these challenges, our work proves to provide insight into the pressing and critical field of pediatric epilepsy. It

contributes an important step toward understanding the inherently complex nature of epilepsy, offering valuable insights for future research.

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