Epilepsy & Behavior 154 (2024) 109744

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

eDeeplepsy: An artificial neural framework to reveal different brain states in children with epileptic spasms

Alberto Nogales [c], Álvaro J. García-Tejedor [c], Juan Serrano Vara [c], Arturo Ugalde-Canitrot [a,b,*]

[a] School of Medicine. Universidad Francisco de Vitoria, Ctra. M-515 Pozuelo-Majadahonda km. 1,800, Pozuelo de Alarcón 28223, Spain
[b] Epilepsy Unit, Neurology and Clinical Neurophysiology Service, Hospital Universitario La Paz, Paseo de la Castellana, 261, Madrid 28046, Spain
[c] CEIEC Research Institute, Universidad Francisco de Vitoria, Ctra. M-515 Pozuelo-Majadahonda km. 1,800, Pozuelo de Alarcón 28223, Spain

ARTICLE INFO

Keywords:
Artificial Intelligence
Deep Learning
Convolutional Neural Networks
EEG
Seizures
Pediatric Epilepsy

ABSTRACT

Objective: Despite advances, analysis and interpretation of EEG still essentially rely on visual inspection by a super-specialized physician. Considering the vast amount of data that composes the EEG, much of the detail inevitably escapes ordinary human scrutiny. Significant information may not be evident and is missed, and misinterpretation remains a serious problem. Can we develop an artificial intelligence system to accurately and efficiently classify EEG and even reveal novel information? In this study, deep learning techniques and, in particular, Convolutional Neural Networks, have been used to develop a model (which we have named eDeeplepsy) for distinguishing different brain states in children with epilepsy.

Methods: A novel EEG database from a homogenous pediatric population with epileptic spasms beyond infancy was constituted by epileptologists, representing a particularly intriguing seizure type and challenging EEG. The analysis was performed on such samples from long-term video-EEG recordings, previously coded as images showing how different parts of the epileptic brain are distinctly activated during varying states within and around this seizure type.

Results: Results show that not only could eDeeplepsy differentiate ictal from interictal states but also discriminate brain activity between spasms within a cluster from activity away from clusters, usually undifferentiated by visual inspection. Accuracies between 86 % and 94 % were obtained for the proposed use cases.

Significance: We present a model for computer-assisted discrimination that can consistently detect subtle differences in the various brain states of children with epileptic spasms, and which can be used in other settings in epilepsy with the purpose of reducing workload and discrepancies or misinterpretations. The research also reveals previously undisclosed information that allows for a better understanding of the pathophysiology and evolving characteristics of this particular seizure type. It does so by documenting a different state (*interspasms*) that indicates a potentially non-standard signal with distinctive epileptogenicity at that period.

1. Introduction

Artificial intelligence (AI) is currently undergoing exciting growth in many quotidian aspects of life and of course in the medical field. Major advances have already been attained, especially in the imaging arena. A renowned example is the capability of AI systems to be non-inferior or even surpass human experts in breast cancer prediction through interpretation of screening mammography [1].

The complex analysis and interpretation of electroencephalograms (EEG) still essentially rely on visual inspection by a super-specialized physician. Accurate identification of abnormalities heavily depends on experts with extensive clinical experience that usually have a nonlinear working method that is highly time-consuming and requires careful inspection, creativity, and problem-solving skills. However, even in the best of scenarios, some cases escape human perception and could be assisted and complemented by new technologies that efficiently circumvent difficulties humans may not be capable of solving. Most importantly, they can help reveal patterns that have previously not been identified and that can help in understanding pathophysiological processes with ultimately relevant diagnostic, therapeutic and prognostic applications.

In this sense, computational modeling and artificial intelligence have

---

* Corresponding author.
E-mail addresses: alberto.nogales@ceiec.es (A. Nogales), a.gtejedor@ceiec.es (Á.J. García-Tejedor), juanjose.serrano@ceiec.es (J. Serrano Vara), a.ugalde.prof@ufv.es (A. Ugalde-Canitrot).

https://doi.org/10.1016/j.yebeh.2024.109744
Received 4 December 2023; Received in revised form 11 February 2024; Accepted 10 March 2024

already proven to be necessary tools in the study of epilepsy [2]. Among them, deep learning methods were introduced as hierarchical models that can learn data representations with multiple levels of abstraction [3]. In this study, deep learning techniques and, in particular, Convolutional Neural Networks (CNN), have been used to develop a model (which we have named eDeeplepsy) for distinguishing different brain states in children with epilepsy. CNN are a deep learning model designed to analyze data exhibiting a grid-like structure, such as images. Its architecture draws inspiration from the organization of the visual cortex in animals [4]. CNN are widely recognized for their performance in computer vision due to their ability to process the dimensional information of an image and reduce the amount of information stored in memory for high-resolution images [5]. The decision to use CNN is related to the fact that we are facing an image classification problem and these models have demonstrated a better performance against classical machine learning models [6,7].

The motivation of this work is focused on certainly the most intriguing seizure type, known as epileptic spasms, in particular those occurring beyond the infancy period. One of its most interesting features is that, unlike other epileptic seizures, spasms characteristically appear in clusters, following a pseudo-periodic pattern, lasting several minutes, preferably upon awakening from sleep. This means that once a cluster begins, multiple spasms will follow at different intervals as if generated by some kind of repetitive loop in the brain [8,9]. It is not well known what exactly is occurring between these spasms within a cluster, and EEG at the time is visually indistinguishable from the background EEG activity of the patient.

Although epileptic spasms have been a well-recognized entity for more than 150 years, the pathophysiology and anatomical brain structures involved in their genesis are still not fully clarified. Little is known about their origin, their unusual EEG correlation, and their peculiar response to medication [10].

There are few papers where deep learning models have been used in epilepsy but none for discriminating the states in the particular case of epileptic spasms raised in this work. In terms of review papers compiling deep learning techniques applied to EEGs, [11] and [12] can be highlighted. Concerning the use of deep learning applied more specifically to epilepsy, [13] uses CNN alongside intracranial EEGs for detecting Interictal Epileptic Discharges. Besides, [14] describes a framework based on CNN to classify different seizures. In [15], CNN are used again but in this case with a 1-dimension approach solving scenarios such as seizure, non-seizure, normal and inter-ictal. A simpler use case of classifying healthy and epileptic patients is made in [16] again using CNN. [17] presents a three-step method: first, it creates artificial preictal EEGs, then it extracts features with Common Spatial Pattern (CSP) and, third, it uses CNN to classify between pre-ictal and inter-ictal states. Finally, a similar approach to the one presented here is [18], which converts EEG into images and analyzes them with CNN, but they do not show brain activity in a scalp representation neither are applied to different use cases of a particular type of epilepsy, as in this paper.

The main objective of this work is to develop and validate an AI system for accurately and efficiently classifying EEG in epilepsy, even in the more complex settings such as that of children with epileptic spasms. The system would need to consistently discriminate and document distinctive brain states in and around seizures. One of the reasons for studying patients with epileptic spasms is because these are among the more subtle seizure types, both clinically and electrically, and are many times difficult to discern. We therefore go some steps further, beyond the systems generally centered on evident seizures such as generalized/bilateral tonic-clonic seizures.

The second objective is to explore whether this AI system is capable not only of classifying into regular EEG categories, by detecting elements such as epileptiform abnormalities and ictal patterns, but also of revealing novel information. It would do so by documenting EEG differences that usually escape human visual inspection but that may actually represent different brain states. Epileptic spasms offer a variety of features above other seizure types. We particularly wanted to differentiate between two brain states: the one between actual epileptic spasms but within a same cluster, from the one outside epileptic spasms or clusters. This indicates a previously unrevealed potentially non-standard signal, perhaps depicting a state of increased epileptogenicity within clusters.

2. Material and methods

2.1. EEG data collection

This study has been performed with a set of retrospectively collected scalp EEG samples obtained from a group of pediatric patients with medically refractory epilepsy in which epileptic spasms had been recorded and classified during video-EEG monitoring at the same level-four epilepsy center (Hospital Universitario La Paz, Madrid). The present research has followed strict recommendations by the hospital Ethics Committee.

For each patient, a set of 25 electrodes was placed on the exact scalp locations according to the standardized 10–10 and 10–20 systems. Data has been collected and processed for these cases using a Nicolet video-EEG machine and associated software, with a 512 Hz sampling rate.

The dataset is created from five pediatric patients (ages 5–11 years), anonymized using identification numbers from 1 to 5. All had structural etiology, four patients with suspected cortical dysplasia and one with destructive lesions due to shaken baby syndrome. No relevant abnormalities were documented in genetic and metabolic studies. Complete long-term video-EEG recordings had been previously analyzed and interpreted by the same clinical neurophysiologist, creating a medical report according to regular clinical practice. The reports were later reviewed and confirmed by a second physician. Patients were monitored during different periods in which multiple epileptic spasms grouped in clusters occurred. A summary of patients' clinical and EEG information is collected in Table 1.

For this study, recordings were again examined and specific segments from different states were carefully selected, manually pruned, and labeled for each patient. Only the segments with the fewest artifacts were selected through expert visual inspection, and passive patient behaviors were sought within those segments (as confirmed through given instructions, patient feedback, and/or concurrent video analysis). It was verified that optimal technical standards were met and that no segments with excess artifacts or atypical conditions underwent computer analysis. Segment duration varied slightly from 3 to 6 s and they were hand-selected by an epileptologist to include homogenous information. Each of the five patients has a set of 98–118 EEG segments, categorized according to the different states defined:

"*Spasms*". The moment in which the epileptic spasm and its concurrent visually identified EEG seizure pattern are recorded.

"*Interspasms with*". The moment between spasms within a cluster with epileptiform abnormalities.

"*Interspasms without*". The moment between spasms within a cluster, without epileptiform abnormalities.

"*Wakefulness with*". State in which the patient is awake, away from seizures, with visible epileptiform abnormalities.

"*Wakefulness without*". The moment of wakefulness, away from seizures, without visible epileptiform abnormalities.

Segments representing "*Interspasms*" and "*Wakefulness*" states were always clearly away ($\geq$5 s) from any preceding or succeeding visually identified ictal pattern, to avoid immediate preictal or postictal phenomena. All segments fulfilling the overall criteria were included for analysis.

2.2. Data transformation

As proposed in [19], EEGs were transformed into a set of chronological images showing brain activity in different areas of the scalp. The

Table 1
Summary of patients' clinical and EEG data.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age at EEG	10 years 6 months	6 years 4 months	11 years 3 months	7 years 2 months	5 years 4 months
Sex	Female	Male	Female	Male	Male
Etiology	Structural, left F-P CD	Structural, left F-T CD	Structural, left F CD	Structural, left F CD	Structural, bilateral destructive lesions (shaken baby syndrome)
Total EEG length (hours)	119	101	125	7	3
Epileptic spasms	75	170	331	40	115
Clusters	14	7	16	7	3

CD: cortical dysplasia; F: frontal; T: temporal; P: parietal.

idea is to separate the signals depending on the relative contribution of each of the three types of primary waves with the highest frequency: theta, alpha, and beta [20]. This information will be used alongside the electrode's position in the scalp to create an RGB (red, green and blue) image, where the contribution of each wave type will be interpreted as the RGB layers of the image and the position of the electrodes will show the area of the scalp where the activity takes place. An image will correspond to a particular instant of the EEG and, to work with all the EEG, a moving time window will generate a set of sequential images.

Preprocessing begins by applying the Fast Fourier Transformation (FFT) [21]. This algorithm allows calculating the Discrete Fourier Transformation (DFT) of a time series and its inverse, inverse DFT. This information can be represented alongside the brain region where it occurs, generating a visual description of neural activity. Since each frequency range can be represented as a channel (red, green, and blue) of an image and, as there are three different types of signals, an RGB image can be created. An example can be seen in Fig. 1 which represents a model of the scalp seen from above (axial representation) and the different colors characterize the brain activity in terms of frequency bands at a given moment and state. In this case, red, green, and blue represent alpha, theta, and beta activity, and the other colors are a mix of different waves.

2.3. Data classification

Once all the EEG segments have been transformed into images, they are classified using Deep Learning techniques. Our proposal is to use a convolutional neural network (CNN) model.

This model introduced in [22] was one of the biggest milestones in image processing. CNN are based on the capabilities given by the convolutional operator, which extracts the main features of an image regardless of its location. This allows recognizing parts of an image that were previously found in another image.

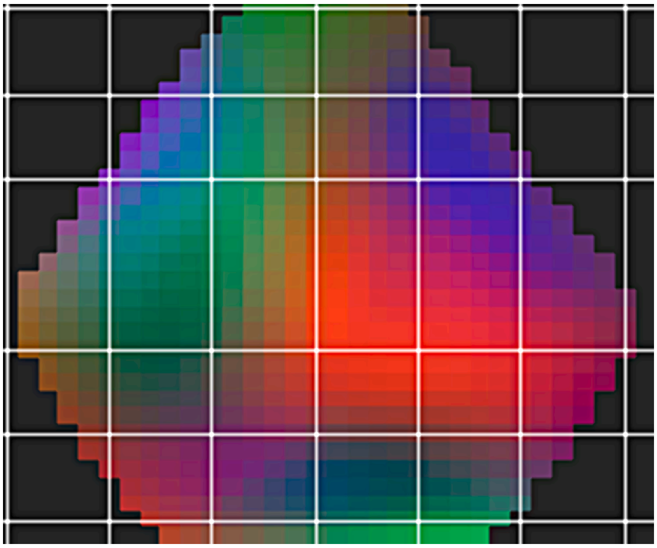

Fig. 1. An example of the scalp-representation model, with type and location of EEG activity.

CNN models consist of an input layer, a series of convolutional blocks, and a classification multilayer perceptron. These convolutional blocks include a convolutional layer and a pooling layer. The blocks are arranged in a stacked manner to extract key features from the image while simultaneously reducing dimensionality to a minimal set with the extracted characteristics. Convolutional layers consist of neurons and their corresponding weights, where each neuron is a matrix of numbers referred to as a filter or kernel. The kernel traverses all input images, calculating an element-wise product, which is then summed up to obtain the output value, as detailed in the equation:

$$Yk = f(Wk^{*}X)$$

In the given equation, X represents the input image, and W_k denotes the filter with the k^{th} feature map, employing the convolutional operator *(*)* on a pixel-wise basis. The outcome of this convolutional operation yields a specific feature corresponding to the image. As the filter traverses the entire image, it produces an activation map output matrix. An essential hyperparameter determined in the training stage is the number and size of kernels.

Subsequently, a pooling operation is applied to facilitate dimensionality reduction. Two types of pooling layers are commonly used: maximum pooling, which identifies the maximum value in the activation map, and mean pooling, which calculates the average of the values.

3. Results

The models developed in this paper have been applied to solve four use cases related to the different brain states:

Use case 1: to determine differences between *"Interspasms without"* and *"Wakefulness without"*. The aim is to discern whether the activity recorded outside a spasm itself but within a cluster of spasms and without epileptiform abnormalities is similar to that away from a cluster, in a wakefulness state without epileptiform abnormalities. This is like examining two different states of normal appearance, which usually remain undifferentiated under expert visual inspection.

Use case 2: to determine the differences between *"Spasms"* and *"Wakefulness with"*. The aim is to distinguish whether the activity observed in and immediately around a spasm (ictal state) is different from that away from a cluster, in a state of wakefulness with epileptiform abnormalities (interictal state). This is like examining ictal and interictal states, which usually (but not always) can be differentiated under visual inspection.

Use case 3: to determine the differences between *"Spasms"* and *"Interspasms with"* categories. The aim is to find out whether the activity observed in and immediately around a spasm (ictal state) is different from that outside a spasm itself but within a cluster and with epileptiform abnormalities (interictal state). This is again like examining ictal and interictal states, although in a different situation, which usually (but not always) can also be differentiated under visual inspection.

Use case 4: to determine the differences between *"Interspasms with"* and "*Wakefulness with*" states. The aim is to find out whether the activity observed outside a spasm itself but within a cluster of spasms and with epileptiform abnormalities is similar to that away from a cluster, in a state of wakefulness with epileptiform abnormalities. This is like examining two different interictal states, which usually remain undifferentiated under visual inspection.

All the results have been obtained by developing a Python script using different libraries: NumPy,[1] which is the fundamental package for scientific programming, pandas,[2] which allows users to manage data structures easily, Matplotlib,[3] providing functions to plot graphs, scikit-learn,[4] which is a package for data mining techniques, and Keras,[5] a framework to implement deep learning models.

3.1. Developing an image classifier

Performances of CNN were obtained, as it is the best approach to work with images. Dataset was split into 80 % for training and 20 % for validation. Before starting to train the model, the training dataset was shuffled randomly and normalized in the ranges of 0 to 1. Table 2 shows the performance of CNN in all cases.

The CNN architecture, two convolutional layers of 25 and 32 neurons respectively with a 3x3 filter with activation functions ReLU and sigmoid, were used. The next layer corresponds to a MaxPooling one with a 2x2 window and a dropout (this allows disconnecting randomly a percentage of neurons to avoid overfitting) of 20 %. Grid search has been used to find the values of the hyperparameters, this strategy tries different combinations of hyperparameters to find the optimal model. After that, a flatten layer was implemented to classify the features obtained in the convolutional stage. Finally, the model is connected with an output layer with two neurons and a SoftMax activation function.

3.2. Comparison between convolutional models

Once it was checked that the proposed CNN (eDeeplepsy) performs well, it was compared with a set of classical CNN architectures. It was decided to use the dataset with AlexNet, VGG16, MobileNet, and DenseNet. AlexNet is well-known, as it was a milestone for CNN field [23]. VGG16 is a 16 blocks convolutional layer architecture obtaining [24]. MobileNet was used in [25] to improve performance in mobile and embedded applications. Finally, DenseNet [26] was also standing out among the state-of-art. In Table 3, these models are compared with the one proposed in this paper. Accuracy and speed performance were measured in the four proposed use cases. As shown, the proposed model obtains the same results in terms of accuracy in almost all situations. There are only a few settings in which this metric is better in other models, but it is however much worse in terms of speed performance.

Table 2
Accuracy in CNN for all cases.

Use Case	CNN validation accuracy (%)
1	91
2	89
3	84
4	81

Table 3
Performance comparison between eDeeplepsy and other convolutional architectures.

Use case	Model	Validation accuracy	Execution time
1	AlexNet	55	6 min 59 sec
	VGG16	**95**	9 min 9 sec
	MobileNet	66	6 min 33 sec
	DenseNet	80	26 min 33 sec
	eDeeplepsy	**94**	**1 min 34 sec**
2	AlexNet	60	12 min 8 sec
	VGG16	**90**	15 min 51 sec
	MobileNet	75	11 min 2 sec
	DenseNet	68	31 min 23 sec
	eDeeplepsy	**90**	**2 min 15 sec**
3	AlexNet	44	10 min 22 sec
	VGG16	**89**	14 min 30 sec
	MobileNet	78	10 min 16 sec
	DenseNet	78	25 min 38 sec
	eDeeplepsy	**86**	**1 min 56 sec**
4	AlexNet	49	12 min 50 sec
	VGG16	**87**	18 min 52 sec
	MobileNet	78	13 min 25 sec
	DenseNet	75	24 min 33 sec
	eDeeplepsy	**87**	**2 min 39 sec**

3.3. Comparison between different training

The order in which the data is shown to the network is of utmost importance, even more so when considering limitations regarding population size. Based on this, the model has been trained in three different ways: regular, retraining, and inverse retraining.

Regular is the mode used to obtain previous results and consists of choosing all patients in incremental order from patients 1 to 4 (when possible) for training and then making the prediction with patient 5. With this training, weights are initialized each time the number of patients is increased. The problem with this training mode is that the knowledge gained from training with previous patients is disregarded.

Retraining is based on using all patients incrementally without initializing the weights at each step. The network is trained with new patients but using a model that has been trained with previous patients. The network is forced to be trained with new data over a previously trained model. When this happens, the network learns from its previous knowledge, augmenting its generalization capacity.

Inverse retraining is similar to retraining mode. In this case, training starts with the last patient and finishes with what was considered the first patient.

Accuracies for training, validation and test were obtained for all use cases. Furthermore, prediction for a new patient (all the EEGs for this patient) was made in each trial. The datasets for training and validation were obtained from 80 %, 20 % of the whole training dataset except one patient, respectively. It was then tested with the data from a new patient (EEGs from a patient that was never used in training). For example, in regular and retraining mode, the prediction was made for patient 4. In the case of inverse retraining, it was made with patient 1. This allows for observing how the network behaves with an EEG activity from an individual that has never been presented to it.

Table 4 shows the results after training the model in different ways, for each use case. It is divided in cases and contains the training mode that was used, patients used at each step of the training, patient used to make the prediction, training accuracy, validation, accuracy, and test accuracy (predicting a new instance of data). For more precise results, use cases were executed ten times and then averages were calculated.

It is confirmed that the best solution involves inverse retraining. For use case 1, it can also be concluded that there are interindividual differences in EEG brain activity. For use case 2 interindividual differences are slightly smaller. For use case 3 differences between patients are not so large. Finally for use case 4 differences between patients are somewhat larger.

---

[1] https://www.numpy.org/.

[2] https://pandas.pydata.org/.

[3] https://matplotlib.org/.

[4] https://scikit-learn.org/stable/.

[5] https://keras.io/.

Table 4
Performance comparisons between different pieces of training of eDeeplepsy, in different use cases.

Training mode	Patient	Predicted Patient	Train. (%)	Valid. (%)	Test (%)
Regular Use case 1	1	5	98.1	97.6	97.3
	1, 2	5	97.7	95.4	96.2
	1, 2, 4	5	96.8	94.5	95.3
	1, 2, 4, 5	–	93.5	91.5	–
Retraining Use case 1	1	5	98.1	96.6	97.8
	1, 2	5	98.2	93.4	95.1
	1, 2, 4	5	98.7	95.3	97.9
	1, 2, 4, 5	–	84.2	81.2	–
Inverse retraining Use case 1	5	1	97.6	84.3	85.2
	5, 4	1	99.1	98.7	99.3
	5, 4, 2	1	96.1	92.6	96.4
	5, 4, 2, 1	–	**97.4**	**94.7**	**–**
Regular Use case 2	1	5	98.2	97.5	97.5
	1, 2	5	97.4	95.7	96.8
	1, 2, 3	5	95.1	93.1	93.6
	1, 2, 3, 4	5	95.7	93.5	93.8
	1, 2, 3, 4, 5	–	90.9	89.1	–
Retraining Use case 2	1	5	99.2	97.6	97.7
	1, 2	5	98.2	95.7	97.6
	1, 2, 3	5	97.9	93.2	93.1
	1, 2, 3, 4	5	98.5	94.3	94.1
	1, 2, 3, 4, 5	–	85.9	82.7	–
Inverse retraining Use case 2	5	1	85.1	83.7	84.2
	5, 4	1	98.1	96.6	97.3
	5, 4, 3	1	98.9	94.4	92.2
	5, 4, 3, 2	1	97.1	94.9	91.7
	5, 4, 3, 2, 1	–	**98.5**	**96.3**	**–**
Regular Use case 3	1	5	96.1	93.9	93.2
	1, 2	5	97.2	93.6	92.4
	1, 2, 3	5	94.2	91.3	92.7
	1, 2, 3, 4	5	91.4	87.7	88.9
	1, 2, 3, 4, 5	–	86.3	84.1	–
Retraining Use case 3	1	5	96.2	93.4	93.6
	1, 2	5	99.5	96.2	97.1
	1, 2, 3	5	97.8	88.5	88.3
	1, 2, 3, 4	5	90.4	84.1	83.1
	1, 2, 3, 4, 5	–	80.7	80.9	–
Inverse retraining Use case 3	5	1	87.6	84.1	88.2
	5, 4	1	97.6	88.3	90.7
	5, 4, 3	1	96.7	87.9	90.4
	5, 4, 3, 2	1	97.2	95.2	96.7
	5, 4, 3, 2, 1	–	**94.9**	**90.3**	**–**
Regular Use case 4	1	5	96.1	91.6	88.9
	1, 2	5	98.4	83.7	86.1
	1, 2, 3	5	88.1	84.2	84.5
	1, 2, 3, 4	5	87.3	83.8	82.8
	1, 2, 3, 4, 5	–	84.4	81.7	82.1
Retraining Use case 4	1	5	95.3	92.3	89.7
	1, 2	5	90.1	79.6	79.3
	1, 2, 3	5	97.3	93.7	90.8
	1, 2, 3, 4	5	90.3	85.1	86.6
	1, 2, 3, 4, 5	–	81.3	79.6	79.8
Inverse retraining Use case 4	5	1	81.5	80.4	81.7
	5, 4	1	97.5	90.3	93.7
	5, 4, 3	1	97.2	94.9	92.5
	5, 4, 3, 2	1	76.9	72.3	74.1
	5, 4, 3, 2, 1	–	**90.7**	**86.2**	**85.8**

3.4. *Evaluating against a baseline model*

Finally, it was decided to validate the proposed neural model against a non-neural baseline model. Support Vector Machine (SVM) was chosen for being a good model that has historically performed well with image classification. This model is defined in [27] as a classifier that aims to find an n-dimensional hyperplane that separates the instances of the dataset. Its performance was compared with the best results provided previously by eDeeplepsy and represented in the Table 5.

3.5. *Discriminating brain states*

In summary, the proposed model (eDeeplepsy) found differences between states for all four use cases studied. Not only could it differentiate ictal from interictal states in pediatric patients with focal onset epileptic spasms (use cases 2 and 3), but also, interestingly, brain activity between spasms within a cluster from activity away from clusters, usually undifferentiated to visual inspection (use cases 1 and 4).

eDeeplepsy performs significantly better than SVM in the four proposed use cases. As a conclusion, it can be stated that the best model is the convolutional one proposed in this paper using inverse retraining.

4. Discussion

There is increasing interest in applying artificial intelligence (AI) tools to epileptology. EEG signals are a natural fit for such analyses, as there are vast quantities of data acquired across large spatial and temporal scales. Towards a more intelligent and efficient clinical implementation, it is of utmost importance for clinicians to get involved and improve their understanding of the methodologies. A key principle of work has been to establish efficient interdisciplinary relations that could guarantee its usefulness in real-world clinical practice.

The study has focused on a particularly demanding and unprecedented example, which consists of trying to differentiate states in the epileptic brain that usually escape visual inspection, beyond ictal/interictal or even *peri*-ictal state discrimination. In particular, we explore a subgroup of pediatric patients with epileptic spasms beyond infancy, of which much remains unexplained. Hundreds of EEG fragments were pruned and labeled by epileptologists according to different brain states, constituting a novel EEG database from this particular patient population, and experts proposed four use cases for this paper.

Here, a binary, as opposed to multiclass, classification approach was preferred, to highlight the importance of differentiating between states that are commonly hard or even impossible to visually discriminate. We concentrate on states that are believed to be different but are usually indistinguishable under visual inspection.

Due to the established good performance of CNN with images, EEG segments were initially transformed into scalp activation images depicting predominant frequency range and scalp topography of brainwaves at particular moments. Furthermore, the impact of the use of spatial locations thanks to 2D convolutional networks for discrimination of EEG states derives from retaining crucial information relating to underlying brain network topology.

When interpreting the results for the proposed use cases, we can summarize:

- EEG activity within a slot of time during seizures ("*Spasms*") was found to be different from that of another slot of time away from spasms, whether inside a cluster ("*Interspams*") or outside a cluster ("*Wakefulness*"). This confirms that spasms activity is different from any other studied interictal state in these patients.

Table 5
Accuracy comparisons between SVM and eDeeplepsy for all cases.

Use Case	SVM validation accuracy (%)	eDeeplepsy validation accuracy (%)
1	80.2	**94.7**
2	68.7	**96.3**
3	65.6	**90.3**
4	68.1	**86.2**

An application for clinical practice relates to automated seizure detection. The innovation here is the possibility of detecting the subtler and more complex seizure type of epileptic spasms. Most seizure detection devices have concentrated on generalized/bilateral tonic-clonic seizures, which is the most evident seizure type both clinically and electroencephalographically speaking, and have not been found as reliable for other seizures [2].

- EEG activity within a slot of time between spasms inside a cluster (*"Interspams"*) was found to be different from that of another slot of time outside a cluster (*"Wakefulness"*). This holds in either state with or without visible epileptiform abnormalities within those slots, meaning the brain is perhaps still behaving differently at that point, regardless of whether it is generating visible interictal activity or not. This finding, which remains previously unreported to our knowledge, is evidence of a potentially non-standard signal that may suggest different epileptogenicity at that period, helping to understand the pathophysiological mechanisms that promote clustering of seizures.

This implies quite a revelation, since epileptologists have always found epileptic spasms a most intriguing seizure type. The tendency to generate one spasm after another, in the form of clusters, with apparently normal EEG activity in between such spasms, did not seem completely logical. Many have hypothesized that an ongoing abnormal encephalographic activity persists throughout the cluster that characterizes the enduring predisposition to generate epileptic spasms within that cluster [28]. This scalp EEG activity must be a very subtle and complex one, at least at the scalp level and for conventional human analysis, since it remains invisible to expert inspection and assessment. In fact, in our work a post-hoc blinded attempt was made to distinguish between these states by visual analysis, and they remained undifferentiated. It is currently not clear whether or not this activity exists, as well as how or where it is generated. Epileptic spasms were initially considered as originating sub-cortically, but a cortical origin has alternatively been suggested, with various structures potentially participating at different levels. We can only speculate if it is more of a postictal or a preictal activity, although it seems more likely to be a different kind of proepileptogenic state, since postictal activity generally decreases the likelihood for a subsequent seizure. Our findings can be further exploited by analyzing various features within these states (for example regarding areas involved and their connectivity) and the transitions between them. This could help gain insight into the pathophysiology and evolving features of this particular seizure type and maybe others, and also perhaps to determine a way to seek a transition to a less epileptogenic state (from the interspasms state to the state between clusters).

Similar appearing visual-interpreted patterns may have largely distinct diagnostic and therapeutic connotations and these may require more than visual inspection to discern. The benefits of revealing and further analyzing this information can have various purposes: documenting such differences, depicting particular clinical profiles, understanding the underlying brain mechanisms involved, and perhaps offering predictive and therapeutic capabilities for epileptic children.

Although unexplored in this paper, many other different brain states could be assessed in the future using EEG signals, both in physiological situations and pathological conditions. This includes, for example, different sleep states in epilepsy patients, diverse vigilance states, or even singular seizure preceding states that may help with seizure prediction [29]. Generating tools that refine the understanding of epilepsy and enhance seizure detection or prediction offer multiple opportunities to tackle epilepsy itself and other related co-morbidities and complications, such as sudden unexpected death in epilepsy (SUDEP) and its prevention [30].

As it has been already stated, some problems may be encountered when classifying states from patients that have never been treated by the artificial model, particularly when focusing on the more subtle differences. Therefore, there is a need for increased patient populations, although this can be difficult in the rarer forms of epilepsy. Furthermore, at the second stage of this research could be the development of a neural model able to classify brain states throughout the recording itself, at the precise moment of occurrence. This could be of great help in close monitoring settings such as intraoperative neurophysiological monitoring, the intensive care unit, the epilepsy monitoring unit, or chronic ambulatory recordings.

The intention is not to substitute an expert electroencephalographer but instead to reduce the workload and perhaps allow for wider implementation of EEG with similar human resources. This would be very relevant in settings where large amounts of data are generated over several days. Furthermore, despite advances, the interpretation of EEG is affected by high rates of misinterpretation that could be reduced by applying these tools and perhaps prompting further analysis by the physician.

5. Conclusion

We have constructed a neural network model (named eDeeplepsy) capable of discriminating different brain states from EEG of epileptic children, creating opportunities for improved knowledge, clinical planning, and management. The resulting architecture is a Convolutional Neural Network built with the highest accuracy and performance, using inverse retraining.

eDeeplepsy differentiates ictal from interictal states in pediatric patients with epileptic spasms in particular, but this could probably be extrapolated to other types of seizures, since epileptic spasms are among the subtlest seizure types, as well as to various other scenarios in the patient with epilepsy.

In addition and most interestingly, the model consistently discriminates brain activity between spasms within a cluster from activity away from clusters, which usually remains indistinguishable to human visual analysis. This is unprecedented and documents the presence of a distinctive brain state that may favor clustering of seizures and which can be a target for treatment. We highlight the significant ability of deep learning to actually reveal hidden data, rather than just putting into practice its more regular automatic classification properties.

6. Ethical publication statement

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

7. Key points

- We present a model for computer-assisted discrimination that consistently detects subtle differences in various brain states of children with epileptic spasms.
- Brain activity between spasms within a cluster is different from that away from clusters, indicating a previously unrevealed potentially non-standard signal.
- We stress the significant ability of deep learning to actually reveal hidden data on EEGs, rather than just its more regular automatic classification properties.

CRediT authorship contribution statement

Alberto Nogales: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Investigation. **Álvaro J. García-Tejedor:** Writing – review & editing, Supervision, Software, Resources, Project administration, Investigation, Conceptualization. **Juan Serrano Vara:** Validation, Software. **Arturo Ugalde-Canitrot:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] McKinney SM, Sieniek M, Godbole V, Godwin J, Antropova N, Ashrafian H, et al. International evaluation of an AI system for breast cancer screening. Nature 2020 Jan;577(7788):89–94.

[2] Abasi B, Goldenholdz DM. Machine learning applications in epilepsy. Epilepsia 2019;60:2037–47.

[3] LeCun Y, Bengio Y, Hinton GE. Deep learning. Nature 2015;521:436–44.

[4] Taye MM. Theoretical understanding of convolutional neural network: concepts, architectures, applications, future directions. Computation 2023;11(3):52.

[5] Dovbnych M, Plechawska-Wójcik M. A comparison of conventional and deep learning methods of image classification. J Comput Sci Inst 2021;21.

[6] Liang, D., Jin, X., Yuan, Y., & Zou, R. (2023, February). Performance Analysis of Machine Learning Methods. In Journal of Physics: Conference Series (Vol. 2428, No. 1, p. 012039). IOP Publishing.

[7] Chen L, Li S, Bai Q, Yang J, Jiang S, Miao Y. Review of image classification algorithms based on convolutional neural networks. Remote Sens (Basel) 2021;13 (22):4712.

[8] Vigevano F, Fusco L, Pachatz C. Neurophysiology of spasms. Brain Develop 2001; 23(7):467–72.

[9] Wilmshurst JM, Ibekwe RC, O'Callaghan FJK. Epileptic spasms—175 Years on: Trying to teach an old dog new tricks. Seizure 2017;44:81–6.

[10] Fusco L, Serino D, Santarone ME. Three different Scenarios for epileptic spasms. Epilepsy Behav 2020;113:107531.

[11] Craik A, He Y, Contreras-Vidal JL. Deep learning for electroencephalogram (EEG) classification tasks: A review. J Neural Eng 2019;16(3):031001.

[12] Roy Y, Banville H, Albuquerque I, Gramfort A, Falk TH, Faubert J. Deep learning-based electroencephalography analysis: a systematic review. J Neural Eng 2019;16 (5):051001.

[13] Antoniades, A., Spyrou, L., Took, C. C., & Sanei, S. (2016, September). Deep learning for epileptic intracranial EEG data. In *2016 IEEE 26th International Workshop on Machine Learning for Signal Processing (MLSP)* (pp. 1-6). IEEE.

[14] Asif, U., Roy, S., Tang, J., & Harrer, S. (2019). SeizureNet: a deep convolutional neural network for accurate seizure type classification and seizure detection. *arXiv preprint arXiv:1903.03232*.

[15] Ullah I, Hussain M, Aboalsamh H. An automated system for epilepsy detection using EEG brain signals based on deep learning approach. Expert Syst Appl 2018; 107:61–71.

[16] Bouaziz, B., Chaari, L., Batatia, H., & Quintero-Rincón, A. (2019). Epileptic Seizure Detection Using a Convolutional Neural Network. In *Digital Health Approach for Predictive, Preventive, Personalised and Participatory Medicine* (pp. 79-86). Springer, Cham.

[17] Zhang Y, Guo Y, Yang P, Chen W, Lo B. Epilepsy seizure prediction on eeg using common spatial pattern and convolutional neural network. IEEE J Biomed Health Inform 2019;24(2):465–74.

[18] Emami A, Kunii N, Matsuo T, Shinozaki T, Kawai K, Takahashi H. Seizure detection by convolutional neural network-based analysis of scalp electroencephalography plot images. NeuroImage: Clinical 2019;22:101684.

[19] Bashivan, P., Rish, I., Yeasin, M. & Codella, N. (2016). Learning Representations from EEG with Deep Recurrent-Convolutional Neural Networks. In Y. Bengio & Y. LeCun (eds.), ICLR.

[20] Bashivan, Pouya, Yeasin, Mohammed, and M., Bidelman Gavin. Single trial prediction of normal and excessive cognitive load through EEG feature fusion. Proceedings of IEEE Signal Processing in Medicine and Biology (SPMB) conference, pp. 1–5, December 2015.

[21] Cochran, W.T., Cooley, J.W., Favin, D.L., Helms, H.D., Kaenel, R.A., Lang, W.W., Maling, G.C., Nelson, D.E., Rader, C.M., & Welch, P.D. (1967). What is the fast Fourier transform.

[22] LeCun, Y., Boser, B. E., Denker, J. S., Henderson, D., Howard, R. E., Hubbard, W. E., & Jackel, L. D. (1990). Handwritten digit recognition with a back-propagation network. In *Advances in neural information processing systems* (pp. 396-404).

[23] Krizhevsky, A., Sutskever, I., & Hinton, G. E. (2012). Imagenet classification with deep convolutional neural networks. In *Advances in neural information processing systems* (pp. 1097-1105).

[24] Simonyan, K., & Zisserman, A. (2015). Very Deep Convolutional Networks for Large-Scale Image Recognition. CoRR, abs/1409.1556.

[25] Howard, A.G., Zhu, M., Chen, B., Kalenichenko, D., Wang, W., Weyand, T., Andreetto, M., & Adam, H. (2017). MobileNets: Efficient Convolutional Neural Networks for Mobile Vision Applications. CoRR, abs/1704.04861.

[26] Huang, G., Liu, Z., Van Der Maaten, L., & Weinberger, K. Q. (2017). Densely connected convolutional networks. In *Proceedings of the IEEE conference on computer vision and pattern recognition* (pp. 4700-4708).

[27] Boser BE, Guyon I, Vapnik V. A training algorithm for optimal margin classifiers. Comput Learn Theory 1992:144–52.

[28] Wilmshurst JM, Ibekwe RC, O'Callaghan FJK. Epileptic spasms – 175 years on: Trying to teach an old dog new tricks. Seizure 2017;44:81–6.

[29] Acharya UR, Hagiwara Y, Adeli H. Automated seizure prediction. Epilepsy Behav 2018;88:251–61.

[30] Ryvlin P, Ciumas C, Wisniewski I, Beniczky S. Wearable devices for sudden unexpected death in epilepsy prevention. Epilepsia 2018;59(S1):61–6.