Electroencephalogram Connectivity for the Diagnosis of Psychogenic Non-epileptic Seizures

Chloe Hinchliffe\textsuperscript{1}, Mahinda Yogarajah\textsuperscript{2}, Lilian Tang\textsuperscript{3}, and Daniel Abasolo\textsuperscript{1} member, IEEE

Abstract—Psychogenic non-epileptic seizures (PNES) are attacks that resemble epilepsy but are not associated with epileptic brain activity and are regularly misdiagnosed. The current gold standard method of diagnosis is expensive and complex. Electroencephalogram (EEG) analysis with machine learning could improve this.

A k-nearest neighbours (kNN) and support vector machine (SVM) were used to classify EEG connectivity measures from 48 patients with PNES and 29 patients with epilepsy. The synchronisation method - correlation or coherence - and the binarisation threshold were defined through experimentation. Ten network parameters were extracted from the synchronisation matrix. The broad, delta, theta, alpha, beta, gamma, and combined ‘all’ frequency bands were compared along with three feature selection methods: the full feature set (no selection), light gradient boosting machine (LGBM) and k-Best.

Coherence was the highest performing synchronisation method and 0.6 was the best coherence threshold. The highest balanced accuracy was 89.74\%, produced by combining all six frequency bands and selecting features with LGBM, classified by the SVM. This method returned a comparatively high accuracy but at a high computation cost. Future research should focus on identifying specific frequency bands and network parameters to reduce this cost.

Clinical relevance - This study found that EEG connectivity and machine learning methods can be used to differentiate PNES from epilepsy using interictal recordings to a high accuracy. Thus, this method could be an effective tool in assisting clinicians in PNES diagnosis without a video-EEG recording of a habitual seizure.

I. INTRODUCTION

Psychogenic non-epileptic seizures (PNES) clinically resemble epileptic seizures, but are not characterised by epileptic electrical brain activity [1]. Although the condition is almost as prevalent as multiple sclerosis (2-33 per 100,000) [2], [3], PNES is regularly misdiagnosed: people with PNES are not appropriately diagnosed for an average of seven years [4] and approximately 78\% of patients were taking at least one anti-epileptic drug at the time of accurate diagnosis [5]. This has serious adverse effects for both patients and healthcare systems, through unnecessary visits to hospitals, medical tests, and treatments.

The current gold standard method of diagnosis is the recording of ictal activity (a patient’s typical event) with video electroencephalogram (EEG), from which a specialist assesses the clinically observable features of the seizure and visually inspects the EEG [6]. Although this method is reliable, this diagnostic tool is costly, inconvenient for the patient and not accessible to all hospitals [3].

A potential solution to reduce these problems is machine learning applied to interictal EEG, as it removes the requirement for video recording a seizure to assist a specialist. EEG connectivity has been a point of interest for researchers as a means for improving understanding of PNES [7]. Machine learning techniques have been used to analyse EEG connectivity in PNES patients in previous studies. Xu et al. [8] extracted the clustering coefficient and shortest path length from the coherence matrix, as well as common spatial pattern analysis of the matrix. These two feature sets trained a Fisher discriminant analysis (FDA), and support vector machine (SVM). A t-test revealed little difference between the network properties of the two groups, and low classification accuracies. The classifiers’ highest accuracy was 72\% with the FDA in the theta band. However, the alpha, beta, gamma and broad bands returned lower accuracies of 40-56\%. The common spatial pattern extracted from the brain network topology (SPN) features generally outperformed the network properties and had a highest accuracy of 92\% for the SVM.

Barzegaran et al. [9] studied lagged functional connectivity matrices. The researchers found weakened connectivity centred on the basal ganglia and the linear discriminant analysis (LDA) analysis had an accuracy of 67\%. Ahmadi et al. [10] used clustering coefficient, strength, betweenness centrality, eigenvector centrality, and largest eigenvalue extracted from the correlation matrix. A linear SVM, a radial basis function (RBF)-SVM, a gradient boosting machine, a decision tree and random forest classified the features. When the features were tested individually ”the results were poor”, so they were combined with other EEG measures. This improved the classification, with a highest accuracy of 63.8\%. In Cao et al. [11], the weighted matrix values were trained and tested by a k-nearest neighbours (kNN) classifier. The best classification result was 74.44\%.

The aim of this investigation is to explore the use of machine learning applied to EEG connectivity as a tool in diagnosing PNES.
II. MATERIALS AND METHODS

The data set used was collected at St George’s Hospital, London, following the approval from the local ethics committee. The data included interictal surface EEG recordings from 48 PNES and 29 epilepsy patients. The subjects were diagnosed as either PNES or epilepsy by an expert clinician. The PNES subjects have an age range of 17-59 (mean 34.76±10.55) and a male/female ratio of 14/34. The epilepsy subjects have an age range of 19-79 (mean 38.95±13.93) and a male/female ratio of 18/11. The recordings were taken with Natus Networks with an EEG32 headbox and the EEG electrodes were placed according to the 10-20 system montage. The data were inspected by experienced clinicians in the field, who isolated at least two 15 minute time frames per subject that contained less noise.

The EEGs with a sampling rate over 256 Hz were downsampled to this value. The individual frames were filtered using a finite impulse response (FIR), Hamming window, bandpass filter to give the broadband (0.5-40 Hz) and were then segmented into 10 second non-overlapping epochs. To remove noise, AutoReject [12] was used to automatically remove epochs with noisy EEG. This gave 10452 samples for the full data set. All samples were filtered using the FIR filter into the frequency bands: delta 0.5-4 Hz, theta 4-8 Hz, alpha 8-13 Hz, beta 13-30 Hz, and gamma 30-40 Hz.

EEG connectivity is found by calculating the weighted adjacency matrix of the channels in an EEG segment [10]. The weighted adjacency matrix is found by mapping the synchronisation of each channel pair. A collection of features can then be extracted from this weighted matrix or a threshold binarised version, as seen in Figure 1. The EEG connectivity features used throughout this study were: degree, strength, density, clustering coefficient, local efficiency, global efficiency, modularity, modularity maximum structure, betweenness centrality, and eigenvector centrality. This gave 143 input features per frequency band.

The synchronisation method for building the adjacency matrix and the binarisation threshold can have a significant impact on the reliability of the network. To define these parameters, 10 PNES and 10 epilepsy subjects were randomly selected for experimentation. Two popular methods for calculating the synchronisation were tested across the bands: correlation and coherence. Nine different thresholds and the weighted matrix were also tested: 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9. The connectivity features were extracted from all six frequency bands, including the broadband. These 27 feature sets were randomly undersampled to balance the number of samples in each class, and classified using an SVM with an RBF kernel and a kNN. The preprocessing, and training and testing of the models were implemented using scikit-learn [13]. Coherence with a threshold of 0.6 returned the highest average accuracy and was therefore used in the analysis of the full EEG data set (all subjects).

Feature selection has shown to be an effective method to improve classifiers diagnosing PNES [10], [14]. Two methods of feature selection were chosen based on their opposing techniques: the first used correlation and tree analysis to remove the unhelpful features; and the second ranked using statistical analysis and chose the k-best features. The first method used feature-selector [15], which found the correlation of each feature pair combination and ranked the features using a light gradient boosting machine (LGBM). Features above the 0.95 correlation threshold or that did not contribute to 0.95 cumulative importance in the feature ranking were removed. The second method (k-best) ranked the features based on the ANOVA F-value between the label and feature, and selected the best 40 features. These two
methods were compared to the full feature set. Principal component analysis (PCA) was applied to further reduce the input dimension, giving an average of 57.2±4.2 and 14.5±2.5 inputs per band for LGBM and k-best respectively. For the full feature set, this was the only feature reduction implemented, giving an average of 62.6±2.0 inputs. The feature selection methods were used for all six frequency bands individually, and in combination to give the ‘all’ band, with 858 features reduced to 329.2, 255.6, and 14.8 by the full, LGBM, and k-best methods with PCA.

The SVM and kNN classifiers were evaluated using 10-fold cross validation. Due to an imbalanced data set, with about a third more PNES samples than epilepsy, the feature set was oversampled with synthetic minority over-sampling technique (SMOTE). Furthermore, the models were evaluated with balanced accuracy, as defined in (1) [16], since it avoids inflated performance on the imbalanced classes of the test set. The reported accuracies are the average over the 10 folds.

\[
\text{balanced accuracy} = \frac{1}{2} \left( \frac{TP}{TP+FN} + \frac{TN}{TN+FP} \right) \tag{1}
\]

In equation (1), \(TP\) is the true positive rate, \(FN\) is the false negative rate, \(TN\) is the true negative rate, and \(FP\) is the false positive rate.

III. RESULTS

When defining the parameters, coherence significantly outperformed correlation with mean accuracies of 90.60% and 77.98% respectively. The coherence with a threshold of 0.6 returned the highest average accuracy: 92.46%. These parameters were then used to analyse the full data set, the classification accuracies of which are reported in Tables I and II.

The balanced accuracies of the SVM and kNN classifiers are shown in Table I and Table II, respectively. The tables show that each combination had diagnostic capabilities, with all accuracies over 65.00%, with two combinations returning accuracies over 80% for each classifier. The highest accuracy was 89.74%, with 91.17% precision and 93.17% recall, produced by the combination of all frequency bands and LGBM feature reduction classified by the SVM.

The combination of the frequency bands in ‘all’ shows a significant improvement for both classifiers. Without combination the balanced accuracy is highest for broadband but by combining all bands together the accuracy increases significantly. The two bands that returned the lowest accuracies for both classifiers were delta and gamma.

Using the full feature set without feature selection returned the highest mean balanced accuracy for the SVM classifier, but for kNN, LGBM returned the highest mean accuracy. The weakest feature selection method was k-Best, returning the highest accuracy for only one band for one classifier (delta for the kNN). The mean balanced accuracy for k-Best was significantly lower than the other two methods, especially for the SVM.

Although there is little difference between the overall balanced accuracies for the two classifiers, the SVM significantly improved the outcome of the feature set with no selection, compared to kNN. The SVM also improved the best combination (all frequency bands with LGBM feature selection). However, the kNN outperformed the SVM when k-Best feature selection was used.

IV. DISCUSSION

Previous researchers have used EEG connectivity to investigate the underlying pathology of PNES and most found a difference between PNES and epilepsy or healthy controls [20], [21], [22]. Notably, a systematic review of EEG connectivity in PNES found that abnormal connectivity may be involved in the pathophysiology of PNES [7]. Investigators have also used machine learning to explore the diagnostic abilities of EEG connectivity [8], [9], [10], [11]. However, there are inconsistencies in methods of the literature. Most notably that [9] and [11] both differentiated PNES from healthy controls, where [8], [10], and the current study used epilepsy subjects. This impacts analysis of the literature, since it is unclear if a finding is applicable to discerning PNES from only epilepsy, only healthy controls, or both.

The current literature has used fairly small populations at 10 [10], 29 [11], 30 [8], and 36 [9]. The current study has used a significantly larger data set with 77 total subjects. The subjects for [8] and [9] were age- and sex-matched,
where as [11] had a similar age distribution and proportion of male to female, and [10] did not clarify. The current study, however, had a similar age distribution for the two classes but a significant difference in the male to female ratio. These factors can impact the brain networks [18], [19]. Furthermore, the systematic review [7] concluded that subjects should also be comorbidity-matched, since disorders such as depression are prevalent in PNES [17] and can affect the brain networks. However, comorbidity-matching was not done by any study, the current one included. While the lack of age-, sex-, and comorbidity-matching is a limitation of the current study, and may have slightly inflated the accuracies, the trends are still valid.

Furthermore, when comparing the accuracies from the parameter definition and the full data set, the 20-subject group returned a higher accuracy, 92.46%, than the larger data set. The equivalents from the full data set returned accuracies of 78.69% and 77.53% for the SVM and kNN respectively. This is likely due to a high subject variability, which reduced the accuracy of the full data set with outlier subjects.

Although feature reduction is typically an effective method for improving classifiers, the current study found selection only slightly improved accuracy, if at all. This is especially true for the SVM, which generally did better with more features in comparison to the kNN. This implies that more information is generally better. Other researchers used a limited number of inputs for the classifiers, using two [8] or five [10] parameters, or the connectivity matrix itself [9], [11], compared to 10 network parameters for this method.

The combination of the frequency bands is a novel approach for machine learning classification of PNES with EEG connectivity and since relevant information was found in every band it significantly increased the model performance. However, this method is likely amongst the most computationally costly in the literature. Therefore future research should focus on identifying the optimum frequency bands and network parameters to reduce this cost. Further research should also use age-, sex- and comorbidity-matched subjects and differentiate PNES, epilepsy, and healthy controls to explore their relationships.

ACKNOWLEDGEMENT

Thank you to Dr Mahinda Yogarajah and St George’s Hospital, London for the provision of the data. And thank you to the University of Surrey Doctoral College for funding Chloe Hinchliffe’s PhD studies.

REFERENCES