Modelling and Prediction of Pain Related Neural Firings Using Deep Learning

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***Abstract*— We propose a deep learning approach to model and predict pain related neural firings from EEG data. In particular, we target for the first time differentiation between acute and chronic pain. Our modelling strategy followed three steps: 1) Feature extraction of EEG data using Petrosian Fractal Dimension (PFD) and Hjorth activity functions. 2) Source localization of neural firings to differentiate between acute and chronic pain. 3) Modelling and training of a deep learning model for the prediction of the related pain according to the feature extracted neural firings. Based on our results, an occipital brain activation for chronic pain and a temporal activation in the case of acute pain were recognized. Moreover, our long short-term memory (LSTM) based prediction model achieved an accuracy of 91.29% for identification of related pain. The performance of the model was evaluated using precision, recall and F1 scores. For acute pain it achieved scores of 0.90, 0.82, 0.86 and for chronic pain scores of 0.86, 0.93, 0.89 respectively. It is concluded that our approach not only shows better predictive accuracy than the results reported by previous studies, but also represents an important step towards identifying and evaluating pain when patients are incapable of self-reporting it or when the clinical observations are unobtainable or unreliable.**

***Keywords*— Acute pain, Chronic pain, Deep learning, EEG, LSTM, Source Localization.**

I. Introduction

Pain is considered to be a highly unpleasant, uncomfortable sensual and emotional experience. It can be a nuisance like a small headache and will range from mild to severe. This varies in intensity from person to person and therefore it can be considered a highly personal experience. Pain can be classified based on their duration; acute (develops suddenly and lasts for a short time period) and chronic (continuing sensations that last for several months or years) and based on the pathophysiological mechanism; Neuropathic pain, Nociceptive pain and Radicular pain [1]. The pain mechanism is based on the nervous system, the spinal cord and the brain [2].

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When we experience pain, our body sensors pass a message via nerves to the spinal cord onto the brain. The sensation of the pain is registered and processed by the brain thus resulting in an uncomfortable sensation that is often accompanied with an emotional connotation.

Commonly pain is tracked by clinical observations or self-reports [3]. However, when both are unobtainable or unreliable, it becomes more difficult to properly diagnose and treat pain. A study found that even if the pain is considered intolerable, 1 out of 10 patients will not self-report the seriousness of the pain. This represents major queries and worries about the people who are unable to convey their pain at all [3]. In this context, machine learning has been deemed relevant for the advancement of neuroimaging methods in the learning of pain [4], due that it may ensure that nobody is unknowingly suffering and that no unnecessary health complications and superfluous distress occur due to poor identification of pain, which translates into improvement of patient's outcome and quality of life.

The non-invasive neuroimaging technique known as Electroencephalography (EEG) has been used in this study because of its high temporal resolution, clinical ease, and less cost when setting up and maintaining the equipment [2]. EEG is used to extract the complexity of pain patterns by getting exploitable information that is important to generate new knowledge and models based on clinical and experimental data. Our pain prediction models were set up as a classification problem with pain-related data to recognize a specific type of pain (acute or chronic) and used to make predictions about the type of pain based on neurophysiological characteristics present in the data. Importantly, Brown et al. [5] used a support vector machine classifier in fMRI data to categorize non-painful and painful sensation achieving an accuracy of 81%. A naive Bayes classifier used by Huang et al. [6] in EEG data achieved 86.3% accuracy while trying to forecast high and low laser-evoked pain responses. Such studies already showed the plausibility to classify and identify different types of pain in humans by tracking neurophysiological responses for instance through machine learning.

Turk et al. [7], Tawfic et al. [8], and Bromley et al. [9] showed the importance of identifying pain in the early stages. The newly established field of pain research provides modern techniques to analyse pain through complex pain-related data in combination with computer-based processing algorithms that rely on the principles of learning also referred to as "intelligent" algorithms [10]. There is a

neuroimaging review and bioelectric signal processing [11]; Hu et al. [12] integrated CNN and SVM for classification and extraction of features from EEG signals. To extract features from raw EEG signals, a six convolutional layered CNN architecture was used by Khan et al. [15]. Furthermore, a research team led by Ahmedt Aristizabal et al. developed a model that was used to identify the risk of schizophrenia in children by using EEG responses and R-CNN hybrid model [18]. This procedure outclasses traditional feature extraction with a large dataset, and machine learning techniques in image identification and pattern detection in terms of classification accuracy [12].

The aims of the present study are: (1) Characterizing the EEG neural firings of a person according to acute and chronic pain. (2) Identifying different pain conditions and relevant frequency bands of the neural firings, (3) Classifying and assembling these frequency bands with the same response and localizing those according to their activation regions in the brain, (4) Identification and prediction of pain type in relation to the particular neural firing using deep learning.

The goal of identifying whether pain is acute or chronic is vital because when there is a transition from one type to another, the pain mechanism of action is susceptible to change to centralized from peripheral. This is problematic as the threshold for pain stimulus is reduced giving place to dysfunctional pain. Consequently, the outcome of the proposed model can be helpful in providing early treatment to patients accordingly with medicines, surgery and therapies. Every chronic pain was once acute. Therefore, by focusing on this transition it is possible to identify crucial characteristics that assist medical practitioners to forecast when acute pain will become chronic. Using this new approach of deep learning algorithms, it would be possible to get a better accuracy of these predictions based on neurophysiological data in comparison to the one achieved through traditional diagnostic tools.

Previous studies of pain detection, using neuroimaging techniques, relied on the use of SVM, Naïve Bayes, Random Forest and KNN classification methods to classify signatures of pain. To the best of our knowledge, this is the first study that proposes a deep learning model to differentiate between acute and chronic pain on the basis of EEG data.

The paper consists of five sections: the first contains the introduction, the second includes previous works performed in relation to pain, the third includes the details of the proposed model and the architecture, the fourth section contains the results and evaluations of the proposed model and finally the fifth section provides the conclusions on key findings of the research study.

II. LITERATURE REVIEW

This review is conducted mainly on three domains, namely acute pain-based models, chronic pain-based models and deep learning-based models. Her, we focus on different models related to EEG pain studies and provide an insight into the proposed solutions by identifying the strengths and weaknesses of each methodology.

A. Acute Pain based models

In 2011, Schulz et al. [19] performed a study on EEG responses by applying the multivariate pattern analysis (MVPA) to pain (laser stimuli), in order to show that it can be used to identify various levels of non-pain and painful simulations depending on EEG signals which were taken by changing the EEG responses to time-frequency representation by applying a single-trial Hamming attenuated, moving window short time Fast Fourier Transformation. This has given an accuracy of 83%. This has proven that a significant high accuracy can be obtained for classification when the time-spectral pattern of single trial responses was considered and shows the possibility of classifying acute pain EEG responses using machine learning algorithms. However, the authors only considered a simplified pain sensitivity dichotomous model and temporal-spectral responses by disregarding the spatial pattern responses.

In [20], Misra et al. researched on high density EEG responses from prefrontal cortex and contralateral sensorimotor cortex areas of the brain related to pain (heat-evoked) to check if these data are helpful in classifying pain states as high and low using Support Vector Machine (SVM). For the conversion of time domain EEG data to time-frequency domain, Sinusoidal wavelet transform was used. Separation of classes was done using SVM with the Gaussian (accuracy of 89.58%) and linear kernels (accuracy of 81.25%). The former was used for the final classification as it was found to better classifying the classes. The authors concluded that gamma and beta features contribute the most to the classification accuracy. The two validation tests conducted in the study, namely cross-subject analysis and within-subjects analysis, reached a classification accuracy of 70% and 79% respectively.

In [21], Lancaster et al, targeted decoding of acute pain with combined EEG and physiological Data. This study aimed to identify non-painful from painful multimodal sensory stimuli. Classification with features being automatically selected has been done using sparse logistic regression (SLR). A 10-fold cross validation as used for the development of the classifier. The two validation tests conducted in this study were cross-subject analysis (accuracy of 70%) and within-subjects analysis (accuracy of 79%).

In [22], Vijayakumar et al, presented a study directed to quantifying and characterizing tonic thermal pain across subjects from EEG data using random forest models. It was conducted in 4 phases such as control phase, tonic pain phase, tolerance determination and pain threshold. Transformation of the signal to the time-frequency domain was done with the Gabor wavelet. The aim of the present study was to create a model that gives the best representation of the classification of pain responses which was achieved with a classification accuracy of 89.45% as the outcome of the study. In order to check the model performance during testing and training, they have used other metrics than classification accuracy such as the confusion matrices that calculated statistics such as Matthews Correlation Coefficient (MCC), F-measure and Balanced Classification

Yu et al. [28] presented a study on diverse frequency band based convolutional networks for tonic cold pain assessment using EEG. The model was able to recognizing tonic cold pain states (severe pain, moderate pain and no pain) objectively called diverse frequency band-based convolutional neural networks (DFB-based ConvNets), which was a novel classification network. The model consisted of 5 convolution max-pooling blocks. The input data was dealt under the 1st block, with 4 standard blocks and a flatten layer following it. Then the fusion of other pipeline derived features with flatten features of the pooling blocks are done by sending it into the concatenation process. After that, the flattened features are sent. Finally, the classification was done by feeding the created vector into a fully-connected network. For assessing the optimal parameters, DFB-ConvNets model used a 10 fold cross validation method to achieve a classification accuracy of 97.37%. A confusion matrix was used to analyse and evaluate the performance of this model and a standard deviation of 0.26% was achieved using gamma, beta and alpha bands. Other performance metrics were also used to analyse the model performance such as precision, specificity, sensitivity, and F1-measure on 20 frequency band combinations. Out of which 10 had the best performance with F1-measure, sensitivity, specificity and precision of 87.43%, 87.43%, 93.72%, and 87.58% respectively.

1)

In contrast to previous studies, the present work aims to differentiate between acute and chronic pain by utilizing not only temporal but spatial information of EEG characteristics under the framework of a deep learning model.

III. MATERIALS AND METHODS

A. Experimental data

The first dataset that used in this research was obtained from the study 'Dynamics of brain function in patients with chronic pain assessed by microstate analysis of resting-state electroencephalography' [29]. This data set included 88 healthy subjects and 101 subjects (32 males; age 58 ±13 years) who suffer from chronic pain of various types, namely 18 subjects with neuropathic pain, 6 with joint pain, 30 with chronic widespread pain, and 47 with chronic back pain. The chronic pain sufferers presented a pain intensity between 4 and 10 within four weeks prior to the experiment. The EEG data utilized correspond to resting state with eyes open and closed.

The second dataset was recorded at the Technical University of Munich, Germany in the study ‘Distinct patterns of brain activity mediate perceptual and motor and autonomic responses to noxious stimuli’ [30]. This was a study that recorded brain activity using electroencephalography (EEG) for assessing autonomic, motor and perceptual responses to guide noxious stimuli. This dataset consisted of 51 right-handed healthy people (25 females; age 27 ± years. Patients with recurrent or current pain or psychiatric or neurological diseases were excluded. The left hand of each participant was provided with 60 painful stimuli using laser stimulation with 600 mJ as the maximum laser energy and 480±40 mJ as the lowest. Stimuli were given with three different painful intensities that is low, medium and high.

B. Data Pre-Processing

For both datasets EEG data pre-processing was performed with a 50 Hz notch filter and 1 Hz high pass filter was added for the purpose of removing noise and artifact detection of the collected EEG data. Data was down-sampled to 500 Hz. Afterwards, Independent Component Analysis (ICA) was applied to recognize the components that represent artifacts of muscle and eye movements in both datasets. Furthermore, the signals that had more than ±100 μV of an amplitude threshold and signals that displayed a gradient steeper than 30 μV/s were excluded from the experiments performed to collect acute and chronic data.

EEG responses from both studies were inspected visually and bad segments were marked. Next, the independent components that represented artifacts were removed from EEG datasets. The bad segments that were marked previously were also removed and subsequently EEG responses were re-referenced to the average reference. FCz served as the reference electrode during recording. Finally, the pre-processed EEG data was exported as a csv format for performing feature extraction.

C. Feature extraction

After pre-processing, features of each dataset were extracted in order to be used in machine learning models. Two types of feature extraction methods have been used to extract the features that describe the characteristics of the EEG signal: petrosian fractal dimension (PFD) and Hjorth feature extraction methods.

EEGlib and Python libraries were used for analysis of electroencephalographic signals. For the use of EEGlib, a python program that extracts features for the given EEGlib data files was implemented. The extracted features were exported to a csv file along with the class labels that were assigned according to the subject type of data file. The class label for a healthy subject was assigned as 0, class label for a chronic pain subject was assigned as 1 and for an acute pain subject was assigned as 2. These class labels were consistently used in supervised learning models.

Fractal dimension features were considered as the first feature extraction method. Complexity of signals can be described by using multiple self-similarity features in fractal geometry. The PFD function is used to extract features from the EEG signal and it operates by translating the signal into a binary sequence by a quick computation of the fractal dimension of a signal [34]. In the binary sequence transformation, if the difference between continuous samples in the time series oversteps a standard deviation value, it is assigned with ‘1’, otherwise assigned '0'. After which the computation of the fractal dimension is done. PFD was applied to all channels in the pre-processed EEG data file from the EEGlib library [33], and it provided the feature calculations for all channels. As above, the extracted features are saved to a csv file along with the class labels using a python program.

For the second feature extraction method, Petrosian Fractal Dimension (PFD) and Hjorth parameters together were considered. The two feature extraction methods have been combined to gain more information and features from the EEG data. There are different methods of showing statistical properties of time domain signals. One such way is Hjorth parameters, which consist of 3 types: Hjorth Mobility, Hjorth Complexity and Hjorth Activity. Hjorth parameters are able to extract valuable information in frequency and time domain via an easy computation [31]. Variance of the time function is given by the Hjorth Activity parameter, which shows whether the activity gives a large/small value in correspondence to number of high frequency components of the signal. PFD and Hjorth have been applied to all the channels in the pre-processed EEG data file from the EEGlib library.

D. EEG Source localization

As it was important to identify whether the neural firings are unique for each acute and chronic pain and from which areas of the brain these neural responses were evoked, we made use of the BrainStorm tool [32] to illustrate source localization for all acute and chronic pain EEG data.

Initially all the data were imported to brainstorm and the analysis was performed as a group analysis by taking the average estimations for the acute and chronic neural evoking responses for all the experiment data. LORETA (low resolution electromagnetic tomography) was used to analyse source mapping within the cortex [33]. When importing the EEG data for source localization analysis, the events related to the pain were imported. For acute pain analysis, we considered the events in which different stimuli applications were applied to the participant and for which the subject recognized and felt pain. For chronic pain since there were no pain stimuli, there were no events. Because of that the chronic data was imported as 10s time interval for source localization analysis.

The EEG channel mapping was added according to the EEG device (for both acute and chronic experiments, BrainVision 64 channel EEG device was used) in order to co-register the neuronal activation with the 3D brain structure. For computing the source localization, sLORETA function has been selected with Minimum norm imaging and constrained source model.

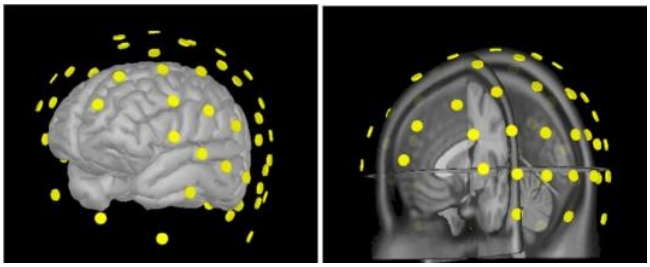

Figure 1: Electrode configuration for brain mapping and 2D imaging.

Average source estimations for both acute and chronic pain data after the creation of the brain images of source localization for all participants was performed for better analysis. First average activation for each subject in the dataset is taken by getting an arithmetic average (mean) for all the events in a single subject. After selecting the averaged data per subject the process pipeline is selected to average all the files of the subjects for the particular pain by using arithmetic average across files, which results in an intra-subject average source localization files which are the average source localization maps (2D, brain maps) for all the participants in the particular pain type.

E. Prediction model

A deep learning neural network model was used for the proposed pain prediction model which is based on Long-Short Term Memory (LSTM) network. An LSTM network has the capability of remembering important information and data for a very long period of time selectively. It is generally used for classification or prediction of sequence or time series data [36].

After feature extraction for all the EEG data participants, an array of data and array of labels were produced where the label array represents the class label i.e. acute pain, chronic pain and healthy participants.

The deep learning model used in this research consists of the input layer, first sequence-to-sequence LSTM layer, a dropout layer with a probability of 0.2, many-to-one LSTM layer, and a dense layer for classification. The first hidden layer contains 64 neurons and uses Relu as an activation function,

$$\mathrm{ReLU}(x) = \max(0, x) \quad (1)$$

The second LSTM layer contains 32 neurons and uses a sigmoid activation function and another dropout layer with a probability of 0.2. The dense layer has used a sigmoid activation function,

$$\mathrm{Sigmoid}(x) = 1/(1+\exp(-x)) \quad (2)$$

The model has been trained on 80% of the feature extracted EEG data using 4 fold cross-validation and tested on 20% of the extracted data.

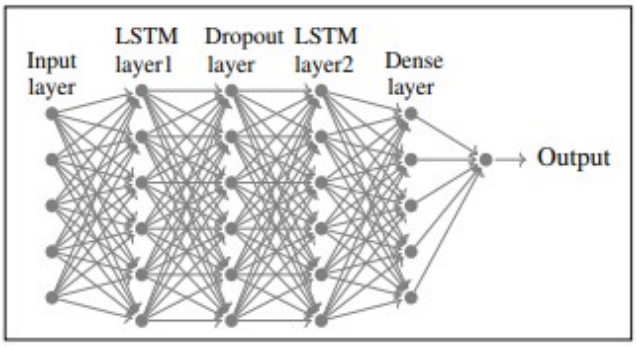

Figure 2: LSTM architecture design

IV. RESULTS AND EVALUATION

A. Source localization

The source localization is performed on the pre-processed EEG data of acute pain subjects as followed,

- Subjects: 51 participants

- Selected event: Highest pain stimulation event (S8)

Figure 3 represents the average event activation 3D brain maps of 6 participants of the acute pain stimulations. It is observed that the middle-left side of the brain has a significant and more activation in all the subjects in the acute pain stimulations.

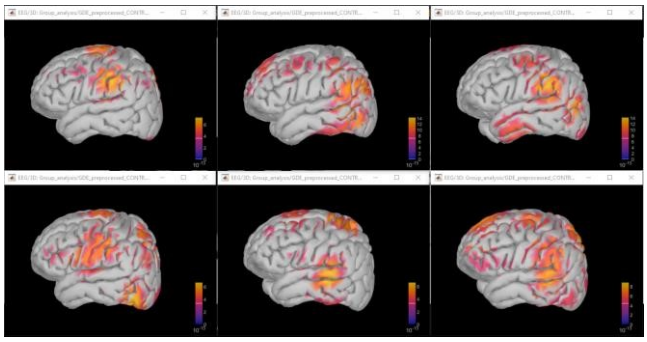

Figure 3: Average event activation 3D brain maps of 6 participants of the acute pain.

Figure 4 represents the overall average activation source localized map for acute pain. From the map, we can observe as described previously the same middle left-brain area has a more significant and high activation for acute pain stimulations. The same results can be observed from Figure 5 representing the overall average 2D map produced for acute pain.

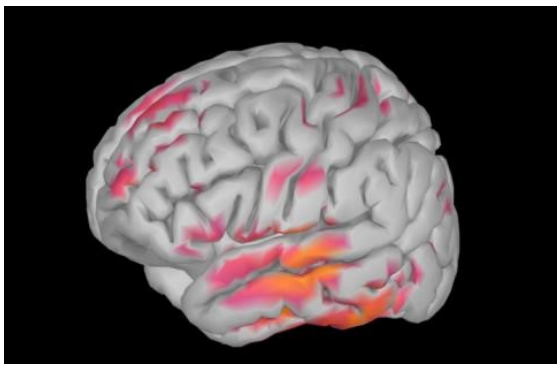

Figure 4: Overall average activation source localized map for all 51 acute pain participants.

Figure 5: Overall average 2D map produced for acute pain.

The source localization is performed on the pre-processes EEG data of chronic pain subjects as followed

- Subjects: 101 patients
- Selected event: Average time response

Figure 6 represents the average neural activation 3D brain maps of 6 participants of the chronic pain sensations. We can see that the middle back side of the brain has a significant activation in all chronic pain patients.

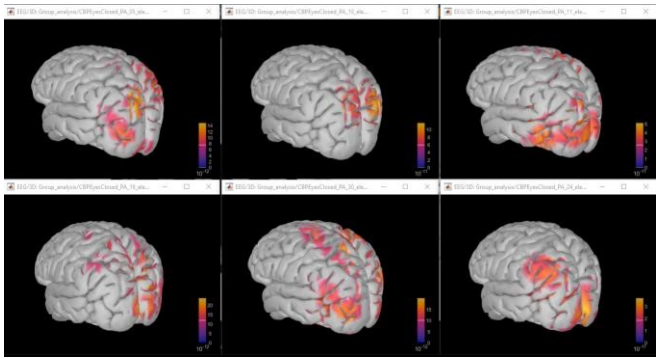

Figure 6: Average neural activation 3D brain maps of 6 participants of the chronic pain.

Figure 7 represents the overall average activation source localized map for chronic pain. From that we can observe as described previously the same middle back area has more significance and high activation for chronic pain patients. The same results can be observed more clearly from the Figure 8 represents the overall average 2D map produced for acute pain.

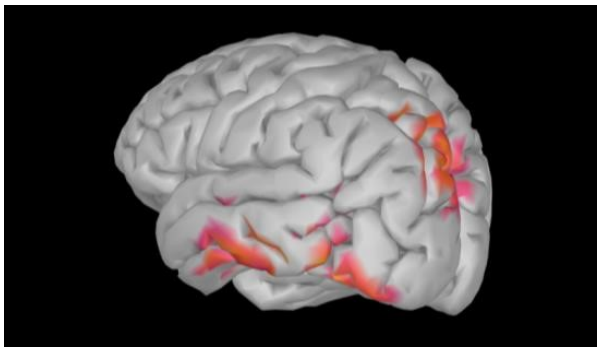

Figure 7: Overall average activation source localized map for all 47 chronic pain patients.

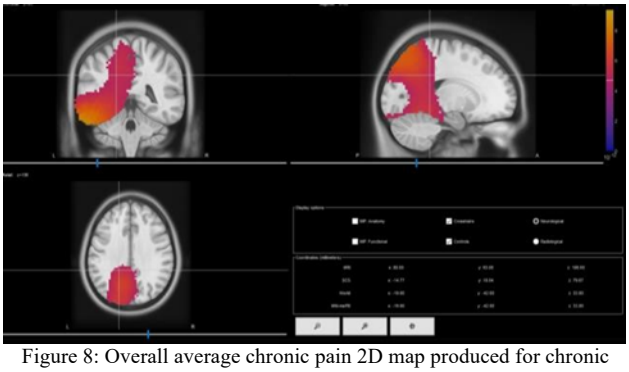

Figure 8: Overall average chronic pain 2D map produced for chronic pain

Comparing between the source localization maps figure 4 and figure 7 we can observe that for acute pain there is more significant activation in the middle (temporal) part of the brain which is more likely towards the left. On the other hand, for chronic pain the middle back (occipital) part of the brain area has significantly more activation. By observing

the 2D source localizations in figure 5 and figure 8 a similar difference is observed from the source localization maps.

B. LSTM based prediction model

The EEG datasets [29, 30] have been used, which consist of 514 subjects in total. Petrosian fractal dimension (PFD) and Hjorth activity functions are used for feature extraction concerning the EEG datasets.

In the training process some epochs produce and train a model which provides more accuracy than the final model. The prediction model is modified to save the highest accuracy model (checkpoint) rather than the final epoch model which might not be the best trained model. Thus, we save and evaluate the best accuracy checkpoint model rather than the final epoch value to get the best accuracy as mentioned in the implementation section.

- Subjects: 514
- Features: 130 Per subject
- Training testing data was split to 80%, 20%
- Cross validation Folds - 4
- Activation function - Relu & Sigmoid
- Loss function - Categorical Cross entropy
- Layer - 3
- Epochs - 500
- With labels for Healthy(0), Chronic(1) and Acute(2)

The model achieved an accuracy of 91.26% after observing the experiment results obtained by the long-short-term memory (LSTM) model with the PFD and Hjorth Activity as feature extraction methods for the dataset using the checkpoint method. The performance values of the model evaluation, namely precision, recall and F1 score for acute pain were 0.90, 0.82, 0.86 and for chronic pain were 0.86, 0.93, 0.89 which represent scores where the model is performing better with high purity and minimum false positive and false negative errors.

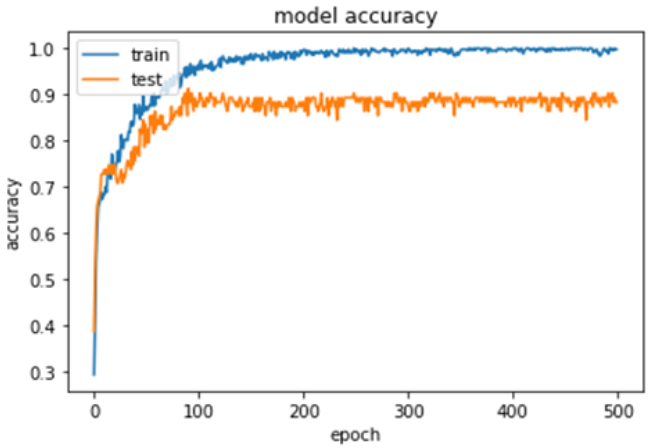

Figure 9: Training and testing accuracy

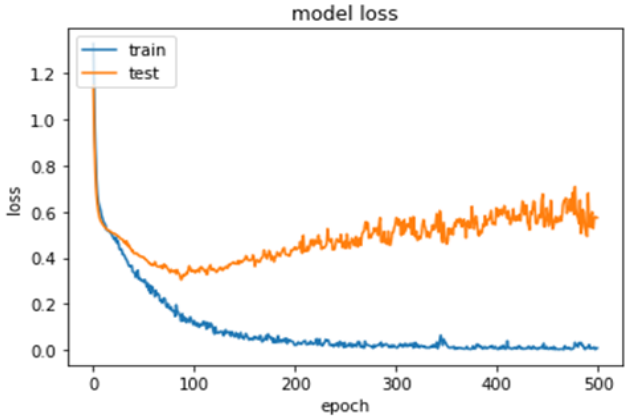

Figure 10: Model Loss in learning process

From figure 10 we can observe that the highest accuracy was achieved at the middle epoch. As shown in table 1 the model achieved a training accuracy of 94.01% and a validation accuracy of 91.26%.

TABLE I
TRAINING AND VALIDATION ACCURACY OF THE LSTM MODEL

	Training Accuracy	Validation Accuracy
LSTM based Prediction model	94.01 %	91.26 %

After the trained model in the evaluation phase with use of the confusion matrix as shown in figure 11 and table II, the observed results are very significant. The healthy participants can be classified with a 100% precision and 100% recall which contains 0 errors. Acute and chronic pain patients were also classified and predicted with significant scores which only contained a very few errors.

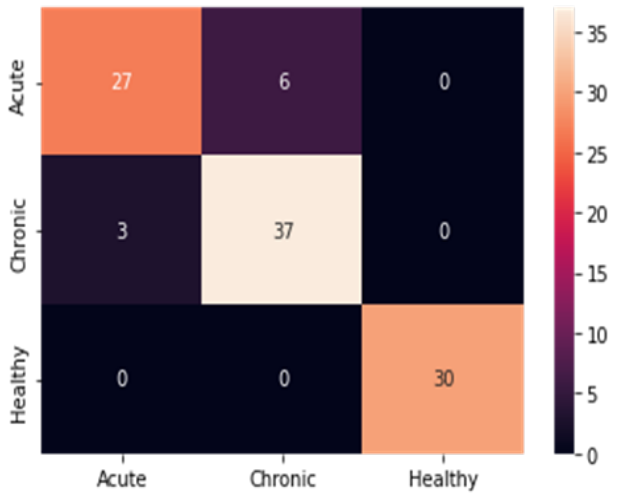

Figure 11: Confusion matrix for EEG pain data of prediction model

TABLE II
PRECISION, RECALL, F1-SCORE AND SUPPORT FOR ACUTE, CHRONIC AND HEALTHY DATA

	Precision	Recall	F1	Support
Acute	0.90	0.82	0.86	33
Chronic	0.86	0.93	0.89	40
Healthy	1.0	1.0	1.0	30

V. CONCLUSIONS

This research addressed the issue of how pain can be assessed in the absence of self-reports and clinical observations and using deep learning techniques in modelling and prediction of chronic and acute pain related neural firings by using EEG data. In this study we proposed a novel approach based on the LSTM model for predicting acute and chronic pain as well as identifying healthy patients. Two feature extraction methods; PFD and Hjorth method, which characterized and extracted the features of the EEG data and enabled categorization of pain based on the neural firings, were used in the training and evaluation of the prediction model. 91.26% accuracy was achieved in pain prediction with the proposed deep learning approach. The observed results are very significant since precision, recall and F1 score for acute pain are 0.90, 0.82, 0.86 and for chronic are 0.86, 0.93, 0.89 which are very good scores where the model is performing better with high purity and very minimum of false positive and false negative errors. This addresses the main goal of the present study, i.e. the prediction of pain through EEG data without any self-report and clinical observation. It has been described and demonstrated that acute and chronic pain can be differentiated using neural firing source localization, where it shows that different areas of the brain were significantly activated for the relative pain sensations. This research has investigated only the classification of pain based on symptom duration, i.e. acute and chronic pain classification. Other types of pain (Radicular, Nociceptive and Neuropathic) were not considered. Therefore, the research can be extended in the future to classify and predict other types of pains; such as Radicular, Nociceptive and Neuropathic pains and to localize these pains that occur through their respective neural firings using source localization.

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