Dynamic Analysis of Human Brain in the Pain State by Electroencephalography

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Research note

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Dynamic Analysis of Human Brain in the Pain State by Electroencephalography

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Abstract

Objective: Pain is an unpleasant sensation that is important in all therapeutic conditions. So far, some studies have focused on pain assessment and cognition through different tests and methods. Considering the occurrence of pain causes, along with the activation of a long network in brain regions, recognizing the dynamical changes of the brain in pain states is helpful for pain detection using the electroencephalogram (EEG) signal. Therefore, the present study addressed the above-mentioned issue by applying EEG at the time of inducing phasic pain.

Results: Phasic pain was produced using coldness and then dynamical features via EEG were analyzed by the Recurrence Quantification Analysis (RQA) method, and finally, the Rough neural network classifier was utilized for achieving accuracy regarding detecting and categorizing pain and non-pain states, which was 95.25$\pm$4%. The simulation results confirmed that cerebral behaviors are detectable during pain. In addition, the high accuracy of the classifier for evaluating the dynamical features of the brain during pain occurrence is one of the most merits of the proposed method. Eventually, pain detection can improve medical methods.

***Keywords*:** Cold pressor test, EEG, Pain, Phasic pain, RQA

Introduction

Considering that pain occurrence activates a long network in the brain regions, the recognition of dynamical changes in the brain leads to pain detection using an electroencephalogram (EEG) at the time of pain induction. EEG is an electrophysiological monitoring technique for registering the electrical activity of the brain [1]. In addition, EEG is mainly used for recognizing sleep disorders, the depth of anesthesia, epilepsy, Alzheimer's, autism, coma, and encephalopathies, and thus it is regarded as a practical method for diagnosing tumors, stroke, and other focal brain disorders [2, 3]. Considering their resulted analysis and using different states, EEG signals help specialists enhance their knowledge regarding the behavioral and functional characteristics of the complex structure in the brain as well [4-7]. Recently, pain detection and its connection with the brain, and pain classification by features have received attention worldwide. Accordingly, the obtained results based on different methods demonstrated that the brain could sense the pain [8-20]. It should be noted that the data in some studies were gathered via EEG. The results of Vatankhah et al. [21,22], Alazrai et al. [23], and Nezam et al. [24] are in line with those of the present study which were obtained based on cold pressor test (CPT), for causing pain to individuals. Mansoor et al. [25] caused pain using coldness and heating stimulus, and differed pain from non-pain states via KNN and SVM classifiers. Panavarnan et al. [26] found that using a hot thermal pad leads to pain in individuals. Misra et al. [27] created pain through thermal stimuli and could classify pain via SVM. Additionally, Vijayakumar et al. [28] caused tonic pain based on the thermal stimulation and then classified the pain. In the present study, EEG data were recorded at the time of pain occurrence and the painless state in order to detect pain. Next, the zero-phase filter was applied for processing and analyzing data and removing the noise. Further, the RQA method was used for extracting the dynamical features of the brain, and finally, the Rough neural network was utilized to classify pain and non-pain states.

Main Text

The remaining sections of the present study are organized as follows. Materials and methods are described in Section 1. Then, Section 2 presents the results, and the main findings are discussed in Section 3.

1. Material and Methods

In this study, the nonlinear features were extracted using the RQA method in order to detect the pain state from the non-pain state. Then, the Rough neural network was applied for pain classification. Figure 1 displays the algorithm of the proposed method.

1.1 Data Acquisition

EEG data were recorded according to the exclusive protocol of EEG, 10-20 standard, 19 channels with a band frequency of 0.1 to 35 Hertz, and the sampling frequency of 500 Hertz. The extensive evaluation was initiated in the Golestan Hospital of Ahvaz after obtaining a license from Ahvaz Jundishapur University of Medical Sciences. Next, the EEG recording in resting and phasic pain (using coldness) states was precisely conducted based on calling for cooperation with ten people including five men and five women were more than 25 years old. Furthermore, they agreed to fill out informed consent for performing this test. Also, they predefined questions both before and after the test. These questions were designed to guarantee that pain in volunteers is detectable and sensible using the Visual Analogue Scale (VAS) method. EEG via the reference method and passive electrodes without any gel has were recorded by the Nihon Kohden electroencephalograph machine, Neurofax model. The main settings in the unit included the activation of the power line filter, and five microvolt sensitivity. The test was performed in a semi-dark room. Volunteers sat down on a chair, and then EEG was recorded in the resting state for 30 seconds. Next, they were asked to put their hands on a cold box until they could tolerate the pain due to the coldness. This process was repeated five times, and the time of pain and non-pain states was recorded accordingly.

1.2 Pre-processing

After EEG recording, the signals of pain and non-pain states were categorized according to the time of occurrence, recording of signal, and sampling frequency (500 Hz). Then, signal processing was performed using Fz, Pz, and Cz channels. Finally, the zero-phase filter was used to remove the noises [29].

1.3 Feature Extraction

RQA is considered as a method of evaluating nonlinear data for applications in dynamical systems. After recording EEG in participants in pain and resting states, features were extracted and data were analyzed using the dynamical analysis of these two states based on EEG signals

and the RQA method. The values of RQA extremely rely on embedded parameters including dimension and delay time. Therefore, 13 features were extracted from the EEG signal as shown in Table 1. Measurement based on the density of recurrence points is the recurrence rate, and measurements such as determinism, averaged diagonal length, the length of the longest diagonal line, and entropy are calculated based on diagonal lines. Furthermore, measurements based on vertical lines include laminarity, trapping time, and the length of the longest vertical line [30-32].

1.4 Apply T-test

A statistical t-test was conducted after extracting features, and P-values were obtained for each feature. The signal classification was performed after applying the t-test and ensuring that features in both pain and non-pain states are different.

1.5 Signal Classification

The Rough neural network is used to classify the signals. These networks are neural structures which include rough neurons [33,34]. The output could be obtained for the second layer (output layer) similar to the multilayer perceptron neural network. Equations (14-20) represent the neural network algorithm.

$$net_L^1 = X \cdot W_L^1 \tag{14}$$

$$net_U^1 = X \cdot W_U^1 \tag{15}$$

$$O_L^1 = min(f^1(net_L^1), f^1(net_U^1)) \tag{16}$$

$$O_U^1 = max(f^1(net_L^1), f^1(net_U^1)) \tag{17}$$

$$O^1 = \frac{O_U^1 - O_L^1}{avrage(O_U^1, O_L^1)} \tag{18}$$

$$net^2 = O^1 \cdot w^2 \tag{19}$$

$$O^2 = f^2(net^2) \tag{20}$$

In this study, the feature matrix had a dimension of 13×60 including 13 rows and 60 columns. Further, the first 30 columns were related to non-pain state data while the second 30 columns belonged to pain state data, which is the input of the neural network. The target matrix was obtained in such a way that features related to resting and pain states had a value of zero and one, respectively. the input of neural network data which was categorized into two sections and in two steps. the first input data were considered as the training data, and the second data as test data,

Then, the second input data were considered as the training data, and the first input data as test data and the classification process was conducted accordingly.

2. Results

In the present study, all P-values in the t-test for 13 features were lower than 0.05, indicating the difference between pain and non-pain states. Therefore, these differences in features demonstrate a sign of the difference in cerebral performance in pain and non-pain states and thus can be used for pain detection and classification in participants. The obtained values from the t-test are presented in Table 1. Next, the accuracy of the Rough neural network classifier was obtained by the confusion matrix [35]. Accuracy value relied on the average and standard division of the values of a confusion matrix using 20 times of the running classifier (Figure 2), which was equal to 95.25±4%. Accordingly, extracting dynamical features and using the neural network based on rough neurons is appropriate for classifying and detecting pain from non-pain states.

3. Discussion

Detection of pain and its differentiation from the non-pain state has globally received special attraction. It should be mentioned that previous studies applied EEG signal processing and its relevant methods for automatic pain detection. For instance, Vatankhah et al. [21,22], Alazrai et al. [23], and Nezam et al. [24] used CPT, similar to the present study, for inducing pain in participants and the data were recorded using EEG. In study by Vatankhah et al. [21], accuracy of the classifier for detecting pain and non-pain states based on nonlinear features was 89 and 93% and based on spectral features, detection accuracy was 75 and 80% using SVM and ANFIS-SVM classifiers, respectively. Vatankhah et al. [22] differentiated pain from the non-pain state based on registered spectral features, and then detected three levels of pain with a wavelet via 95% accuracy. In another study by Alazrai et al. [23], the best accuracy in pain and non-pain detection was 93.86% based on the registered features of the beta frequency band and using the SVM classifier. Nezam et al. [24] could achieve five and three levels of pain in such a way that the accuracy of classifiers with KNN and SVM algorithms was 80±5 and 60±5%, as well as 83±5 and 62±6%, respectively. The advantages of the present study included higher sampling frequency, higher accuracy using the Rough neural network, and nonlinear features. However, separating more levels of pain was the benefit of these studies.

Additionally, Mansoor et al. [25] induced pain using coldness and heat and extracted features from the EEG signal by applying three classes, two classifiers including SVM and KNN, and

achieved 100% accuracy using frequency and time-domain features. Although they used no nonlinear features, their total accuracy was higher compared to the present study. Panavarnan et al. [26], Misra et al. [27], and Vijayakumar et al. [28] inducted pain based on a heating stimulus. In Panavarnan et al. [26] study, high and low power spectral density was observed in alpha and beta, respectively, and the pain was classified based on these features. Additionally, pain and non-pain states were detected by 73.33 and 96.97% accuracy using the linear SVM and polynomial SVM, respectively. In addition, the fuzzy algorithm was used for measuring the pain level (the rate of pain and non-pain states) in different people and had higher accuracy compared to the present study. Furthermore, Misra et al. [27] reported that the pain was classified by analyzing the independent component and localization in EEG references by the density of frequency band pain using SVM with 89.58% accuracy. Therefore, they concluded that an increase in pain sensation is related to an increase in gamma and theta power in the middle prefrontal area and a decrease in beta power in the cortical region, and thus pain is classified based on these features. Finally, the accuracy rate of their study was lower compared to the present study. In a test conducted by Vijayakumar et al. [28], the pain was tonic, and an independent component of the time-frequency wavelet transformation of EEG, and the relative importance of each frequency band using the random forest algorithm was applied, and finally, the accuracy was 89.45%. Using a wavelet, the pain rate was predicted between 0 and 10, demonstrating lower accuracy compared to the present study.

To the best of our knowledge, inducing pain by heating is unsuitable while it has more desirability through coldness. Further, Panavarnan et al. [26], Misra et al. [27], and Nezam et al. [24] reported contradictory results based on the spectral features. Therefore, use alone spectral features from EEG for pain processing are insufficient, and using dynamical and nonlinear features should be considered in future studies.

Nowadays, pain may be present in surgical rooms during anesthesia, which is currently diagnosed by operating room experts due to the difference in the color of patients' faces. The present study aimed to detect pain using the dynamical changes of the brain in order to help people who are unable to express their pain.

Limitations

To the author's knowledge, the present study applied a novel method of pain detection since high accuracy of diagnosis and separation of pain from non-pain states was obtained by analyzing dynamic features using the RQA method and the Rough neural network classifier. It should be mentioned that the test was applied based on phasic pain that inducted by CPT test. In this study only nonlinear features were extracted, and it is suggested that the effect of both linear and nonlinear features be investigated. Furthermore, in this study, the level of pain was not examined.

Abbreviations

Electroencephalogram (EEG); Recurrence Quantification Analysis (RQA); Cold pressor test (CPT); K-nearest neighbor (KNN); Support Vector Machine (SVM); Visual Analogue Scale (VAS)

Declarations

Ethics approval and consent to participate
was waived by the local Ethics Committee of University Islamic Azad University in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

Consent to publish
was obtained from all individual participants included in the study.

Availability of data and materials
Available.

Competing interests
The authors declare that they have no conflict ofinterest.

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Authors' Contributions
All authors contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript

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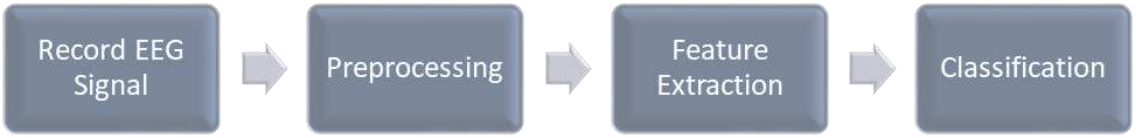

Fig. 1. Algorithm of the proposed method

Table 1. Features and P-value measurements using a t-test for two clusters including pain and non-pain

Number	Features	P-value
1	Recurrence rate	0.0002
2	Determinism	0.03
3	Averaged diagonal length	0.003
4	Length of longest diagonal line	0.008
5	Entropy of diagonal length	0.008
6	Laminarity	0.02
7	Trapping time	0.001
8	Length of longest vertical line	0.0001
9	Recurrence times of first type	0.002
10	Recurrence times of second type	0.02
11	Recurrence period density entropy	0.04
12	Clustering coefficient	0.001
13	Transitivity	4.67E-06

Fig. 2. Error bar based on the mean and standard division of confusion matrix measurements

Note. Blue and orange bars represent the first and second inputs of a neural network, respectively.

Figures

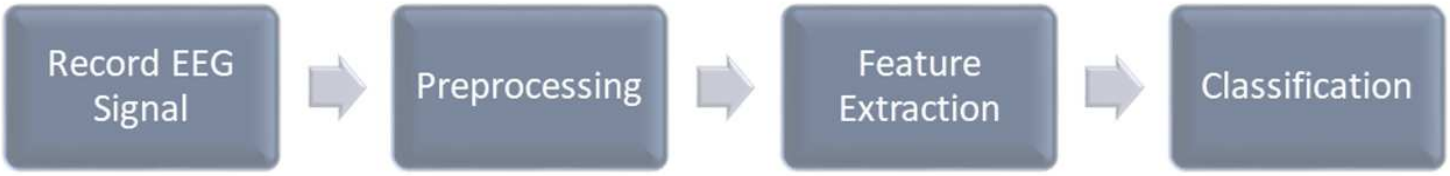

Figure 1

Algorithm of the proposed method

Figure 2

Error bar based on the mean and standard division of confusion matrix measurements Note. Blue and orange bars represent the first and second inputs of a neural network, respectively.