EEG-based discrimination of nociceptive pain generated bylaser stimulation

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Abstract

Nociception is a sensory process provoked by external stimuli that trigger a series of physiological reactions that are experienced as pain. The way it is perceived becomes subjective, as it can vary depending on the emotions and behavior of each person, so analog pain scales have been developed, and new technologies are making an effort to find biomarkers that make these evaluations more quantitative and less subjective. In this research, we propose to detect and classify nociceptive pain caused by applying a transcutaneous laser with 3 different intensities using information from Electroencephalographic (EEG) signals. This study aims to be able to classify between pain and non-pain states of 8 subjects using the biosignals of the database, it also is planned to classify between 3 levels of pain linked in an assumption to the 3 intensities of lasers used as noxious stimuli. The results when classifying pain and non-pain states for each participant are greater than 65% of accuracy.

1. Introduction

Throughout the years, living beings have been evolving and impressively adapting to their environment, and this has been a crucial key to their survival. Much of this process is closely related to a specialized system capable of detecting potentially harmful external stimuli that endanger the individual (Smith & Lewin, 2009). Nociceptive receptors are a series of sensory neurons that can detect changes in temperature, pressure, and chemicals related to dermal damage to protect the individual from harmful stimuli (Dubin & Patapoutian, 2010). These nociceptors acquire information from the environment, and when they find a potentially traumatic stimulus, they send the information in the form of electrical signals that go from the nerve endings, present in most body tissues, to the spinal cord, where the body reacts without consciousness to protect the living being and keep it away from the problem. An example of this is the reflexes, where the muscle stimulated moves without being conscious of wanting to move them. After this, electrical impulses are sent from the spinal cord to the brain where we become aware of what happened and can decide about the event as shown in Fig 1. This nociceptive process is perceived as pain on different levels, so when someone experiences a burn, trauma to the skin, or any contact with corrosive chemicals, the sensation of pain appears.

Pain, manifesting itself in different ways in everybody, caused by different causes and producing different types of pain, becomes complex to assess and characterize. Currently, the most common way to quantify pain is using questionnaires, which to be honest, are easily falsifiable (Celia Vimont, 2019). This does not take into account people with disabilities or in a state of unconsciousness, for whom it is almost impossible to communicate. At the moment, there is a growing number of research aimed at finding a biomarker or pattern related to pain using biosignals and machine learning to detect and quantify it.

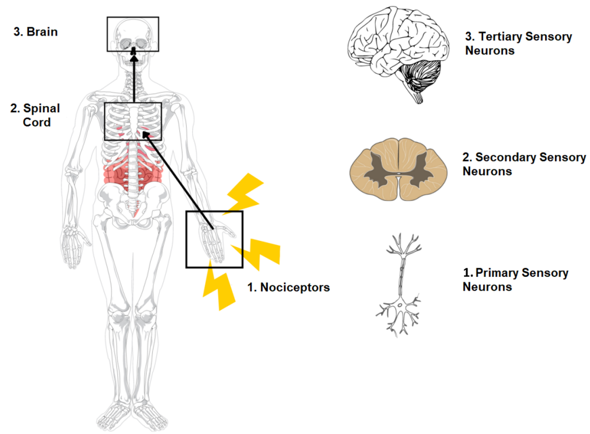

Figure 1. Nociceptive process pathway in humans divided into 3 blocks. Starting with the Nociceptors, then the Spinal Cord, and finally the Brain.

The database used in this work was recorded by (Tiemann et al., 2018). In the work published, she mentioned the fact that pain can be viewed by 3 different types of paradigms. The motor, focuses on the speed with which the body's muscles react to pain. The perceptual, which has to do with the idea that each subject has of the pain, is verbally qualified. The autonomic, which has to do with the sympathetic nervous system, which is what happens in the body without us noticing it, enters the electrocardiogram, to measure the heart rate derived from the pain, and the Skin Conductance

Response, to measure if there is any sweating caused by pain. Technologies such as Electroencephalography (EEG) can be considered to capture these subjective processes that occur in milliseconds by recording the electrical activity of the brain cortex (Subhani et al., 2011; Panavaranan & Wongsawat, 2013; Ramirez et al., 2018). This is important for understanding the physiological response to pain. Therefore, in this research, we propose to analyze the electroencephalographic signal and thus determine the brain response originated by the nociceptors. To conclude, some works currently aim to detect pain using EEG and machine learning (ML) as novel techniques to quantify it and support the medical sector in the way they assess pain. As quantitative pain detection using biological signals continues to develop, the kind of patterns or biomarkers involved are still under debate. Therefore, this research encourages further exploration of this paradigm and hopefully an objective conclusion.

2. Materials and methods

The nociceptive pain database was published by Tieman (Tiemann et al., 2018). This database was recorded with Brain Vision Recorder software (Brain Products), and collected in Germany. They recorded 51 right-handed and completely healthy participants (25 women and 26 men). Their average age is 27 years, the age range is from 20 to 37. This study was approved by the local ethics committee and was conducted with all possible regulations. The following paragraphs detail the protocol used as well as the recording of this database.

2.1. Experimental protocol

The experimental protocol of the database consists of 3 core conditions (perception, motor, and autonomic). In addition to this, a combined condition was recorded, where each of the core conditions was present as can be seen in Fig. 2. The 4 conditions were applied to each participant and consisted of 60 applications of the laser stimulus on the back of the left hand. The laser intensity varied [low=20, medium=20, high=20] in a pseudo-random manner. Between each application of the stimulus, there was a variable time of between 8 to 12 seconds. The perception condition consists of that after each application of the laser, the participant had to verbally state the perception of pain on a scale from 0 to 100. In the case of the motor condition, the participants had to release as quickly as possible a button that they were pressing at the time of starting each application of the stimulus. In the autonomic condition, participants had to focus on the sensation of pain without any other task while the skin conductance response was recorded (SCR). In the combined condition, participants first had to release the button as quickly as possible and then verbally say a number from 1 to 100 in the pain rating, all while the EEG, ECG, and SCR were recorded. Subjects were instructed to keep their eyes closed during the experiments. For this research, only the information of EEG signals is used.

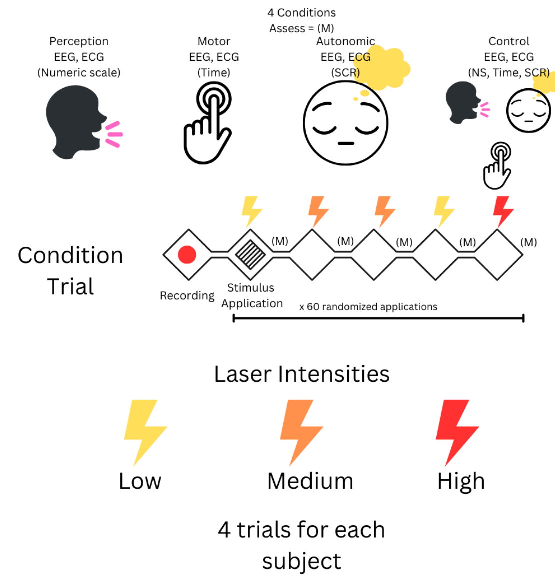

Figure 2. Trials applied to each subject, 60 laser applications were applied in each condition.

2.2. Data Acquisition

EEG data were recorded with an electrode cap (EasyCap, Herrsching, Germany) and BrainAmp MR plus amplifiers (Brain Products, Munich, Germany) using the BrainVision Recorder software (Brain Products, Munich, Germany). The electrode montage included 65 scalp electrodes consisting of all electrodes of the International 10–20 system as well as the additional electrodes FPz, AFz, FCz, CPz, POz, Oz, Iz, AF3/4, F5/6, FC1/2/3/4/5/6, FT7/8/9/10, C1/2/5/6, CP1/2/3/4/5/6, P1/2/5/6, TP7/8/9/10, and PO3/4/7/8/9/10. Two additional electrodes were fixed below the outer canthus of each eye. During the recording, the EEG was referenced to the FCz electrode, grounded at AFz, sampled at 1000 Hz, highpass filtered at 0.015 Hz, and low-pass filtered at 250 Hz. Also, the database has a channel that contains information obtained from an electrocardiogram (ECG) which gives data on the heart rhythm of individuals. Finally, there is a channel for the sensor that measures the skin conductance response (SCR). This gives a total of 65 EEGs, 1 ECG, and 1 SCR channel. It is worth mentioning that of the 65 EEG channels recorded by Tieman, we decided to use only 62 because in many recordings 3 of them fail to be recovered.

3. Methodology

This research focuses on finding a significant difference between pain and no-pain states and the three levels of intensity of the noxious stimulus used (laser) using features extracted from EEG signals recorded in healthy participants.

3.1. Pre-processing

MATLAB R2023a was used for signal pre-processing and feature extraction. Pre-processing is used on the raw signal to clean it of noise (artifacts) and prepare it for feature extraction. On the other hand, it also functions as a method of selection of the usable data. As a first step, the data was downsampled from 1000 Hz to 500 Hz, in this range all oscillations of interest are possibly actionable in compliance with the laws of Nyquist, Theta (4.1-8 Hz), Alpha (8.1-12 Hz), Beta Low (12.5 - 20 Hz), Beta High (20.1 - 31 Hz), and Gamma (31.1 - 60 Hz). This is done to have less time to process the data. Then, a Notch filter of 50 Hz was used This is to eliminate electric line noise.

The EEG databases will be processed along with another biosignal (ECG) to apply independent component analysis (ICA) and to make it easier to remove heart rate-related noise. In addition, electrodes placed under the eyelid will function to eliminate flicker-related noise. After this, the power of each band is obtained from the frequencies mentioned before.

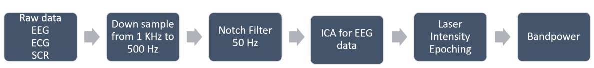

Figure 3. Timeline of the methodology used to preprocess the study data.

3.2. Feature Extraction and Classification

The suggested characteristics were planned to obtain a unique value that would provide sufficient input information to some intelligent algorithm. This is to optimally synthesize the dataset from each data source and reduce the computational processing time. It was decided to obtain the power of each frequency band of interest.

This power is obtained as a single value for each band, and this is obtained for each EEG channel. Therefore, having 6 frequency bands, and 62 recorded channels, at the end 372 characteristics are obtained. This is because each band power is calculated for each laser application, so in a case where all the signal was recorded correctly and no laser application was discarded due to noise in the signal, there should be 20 vectors of 372 characteristics for intensity 1, 20 vectors of 372 characteristics for intensity 2 and 20 vectors of 372 characteristics for intensity 3.

It is worth mentioning that it has also been decided to take a basal state for each of the laser applications. Thus, another 60 instances are added to the ranking matrix. All these with the motive of having information about No Pain. These are calculated in a window of 1 second that happens before applying the laser on the skin of the participants. In the figure 4 you can see how this was applied.

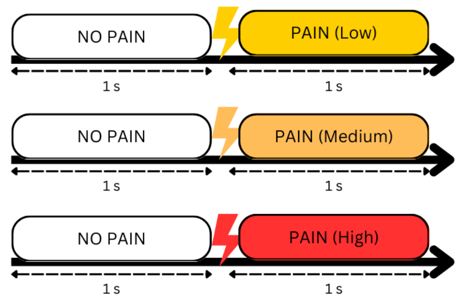

Figure 4. Windowing used in feature extraction.

4. Results and Discussion

Two types of experiments were performed using two different matrices and 4 different learning algorithms. One matrix was built to distinguish between the 3 levels of pain, to know if there is a significant difference between the extracted features. Another of pain with no-pain states, where the 3 levels of pain are characterized and tagged as a single type of pain and the basal states as no pain. For the learning algorithms, 4 models were used. A Support Vector Machine (SVM) of the linear kernel with automatic scaling. For the case of the neural network (NN), a narrow neural network was used, with only 1 layer of connection (10 is the layer size). For the Random Forest algorithm, the maximum number of splits was set as 59. Finally, the K-Nearest Neighbors (KNN) algorithm used a Euclidean distance with only 1 neighbor.

When an attempt was made to distinguish between 3 types of pain (low, medium, and high) in the database of 8 subjects, the algorithms did not perform adequately. The best percentage of highest accuracy was used with Participant 2, using Support Vector Machines, with 54%. Thereafter, all subjects reflect percentages between 30 and 35%, leaving it almost random to identify a type of pain. These results can be seen in the figure 5.

On the other hand, the experiment to distinguish between pain and no-pain states was started by labeling the three levels of pain only as ”Pain”, and the pre-stimulus or baseline state was used as ”No Pain” samples. By doing this, the accuracy percentages improved a lot, now having only 2 labels (Pain and No pain) gives results above 65%. These results can be seen in the figure 5.

Subject	SVM	Neural Network	Random Forest	kNN
S1	41.4	33.2	35.5	29.5
S2	54	43.2	43.7	39.4
S3	33	36.5	42.8	36.45
S4	39.4	42.7	24.1	35
S5	30	35	33.6	31.5
S6	37.8	37.2	46.5	33.45
S7	42	41.8	35.2	38
S8	38.2	29.3	35.6	29.8

Figure 5. Accuracy percentage of the experiment of 3 levels of pain of the 8 subjects using different learning algorithms. In yellow are the best percentages for each subject.

Subject	SVM	Neural Network	Random Forest	kNN	Average Per Subject
S1	77	71	71	67	71.5
S2	68.3	57	65	62	63
S3	80	71	70.2	51	68
S4	74	81.1	67.8	74.5	74.35
S5	76.3	72.8	68	71.5	72.15
S6	57	66.4	62.6	61.6	61.9
S7	63.5	74.2	72.3	69.9	69.975
S8	55.9	61.2	66.4	57.8	60.33
Average Per Model	69	69.3375	67.91	64.4125	(%)

Figure 6. Accuracy percentage of the experiment of Pain and No-Pain of 8 subjects using different learning algorithms. In orange are the best percentages for each subject.

5. Conclusions

At the moment only 8 subjects have been classified using the band power of the EEG signals recorded.

With this, we can say that it is possible to detect if there is pain or not pain using band power information, but it is not possible to distinguish the level of pain experienced. So, what follows with EEG is to find some statistical measures between frequency bands or another kind of feature extraction to know if there is any possibility to make a correct classification between pain levels.

It is also important to mention that we plan to do different independent analyses of the power bands, i.e. alpha only, gamma only, etc. On the other hand, to see if it is possible to distinguish between no pain and each of the pain levels separately, not altogether as it has been done so far. Another proposal is to put all the subjects together to see if there is a good discrimination between pain and non-pain, or is it still individual as to how each being experiences its pain.

The fact of sex, age, and pain threshold does not show any important relation to the fact of good classifications and for the learning models used, kNN never obtained a good percentage of success compared to the other 3. Where SVM and Neural Networks were, in the case of these 8 subjects, the best algorithms for this type of information.

Also, it is important to mention that the article written by (Tiemann et al., 2018), mentions that Gamma is the most significant and participatory power band that is detected when there is pain. They mention that the highest prevalence occurs in the motor test, leading us to believe this behavior could be related to finger movement when removing the button. The perceptual and autonomic tests also show gamma values, although their contribution is minimal.

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