Pain Induction Through Hot Stimuli

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Abstract

Pain is highly subjective and difficult to quantify. The current methods used to assess pain request that the person is able to communicate which is not always possible. This way, automatic classification of pain has emerged, namely using physiological signals. Quantitative sensory testing (QST) is a safe way to induce pain. In this work, a protocol for inducing pain using a thermal QST device was implemented. Three levels of pain (low, medium and high) were calibrated and then induced while recording physiological signals. The results show that features obtained through Electrocardiogram (ECG) and Electrodermal Activity (EDA) could differentiate between pain levels and non-painful states, but could not differentiate well among pain levels.

1 Introduction

Currently, pain quantification is mainly based on self-reporting instruments, such as Numeric Pain Scale (NPS). However, these methods have been shown to be prone to erroneous interpretations. As they rely on a subject's response, is required that the subject is sufficiently alert and cooperative, which is not always possible [4]. Furthermore, pain is a highly subjective and complex phenomenon that is not easy to quantify by the subject itself. Therefore, the interest in an objective assessment and automatic classification of pain has increased. Physiological signals, such as ECG, EMG (Electromyography), and EDA have been used by researchers in order to distinguish between painful and non-painful states or different levels of pain [1, 3].

To study the physiological responses to pain, it needs to be induced in subjects while recording physiological signals. QST is a psychophysical test method that allows to quantify the functional state of the somatosensory system of a tested person based on the response to a controlled stimulus (or stimuli) and it is considered a safe way to induce pain [2].

The aim of this work is to study the physiological response to pain induced by heat, thus the focus is on the thermal QST, using a protocol for pain induction through hot stimuli (using a QST device), while collecting ECG, EMG, and EDA signals. It is expected that the features extracted from the physiological signals present differences among pain levels.

2 Related Works

Several works have assessed pain based on physiological signals.

Treister *et al*. [3] were the firsts to propose a multi-parameter biopotential approach. The authors recorded 3 biomedical signals (ECG, EDA, and photoplethysmography (PPG)) while the heat stimulus was being applied with the thermode attached to the right volar forearm. From these signals, they calculated: Heart Rate (HR) and Heart Rate Variability (HRV) high frequency power from ECG, the amplitude of PPG, and the number of skin conductance fluctuations per minute (NSCF), and Skin Conductance Level (SCL) from EDA. The EDA signal was measured using 2 electrodes positioned on the volar pads of the distal phalanx in the middle and ring fingers of the right hand. Although a total of 55 subjects (21 women and 34 men, ranging in age from 20 to 37 y.o.) completed the study, 10 subjects presented mismatches between pain intensities reported during the calibration period and those reported during the test. For that reason, the data of these subjects were not considered for analysis. Each subject received 4 stimuli: a "no pain" stimulus of 39°C and three individually calibrated stimuli (low pain, medium pain, and high pain). For calibration, a 10 seconds stimulus was delivered with an interval of 1 minute. The first temperature was set at 39°C and it increased 1°C for each consecutive stimulus until the maximum temperature of 48°C. Subjects reported the pain intensity felt (using 0-100 NPS) at the beginning and the end of each stimulus, considering that the pain intensity of each stimulus was the average of both reports. The temperature that caused pain intensity closest to an upper limit of each pain category (30, 60 and 90, respectively) was chosen to be the temperature of the stimulus test for that category. For stimulation, the temperature of the thermode was maintained constant for 60 seconds, and subjects reported their pain sensation every 10 seconds. To assess the differences between the pain categories, non-parametric Friedman tests with post-hoc Wilcoxon signed rank were performed. The authors conclude that all 5 tested parameters successfully differentiated between no pain and other pain categories. However, none of the parameters differentiated between all 3 pain categories, the PPG amplitude and SCL could differentiate between low and medium pain, and all features, except HR, differentiated between low and high pain. Regarding medium and high pain levels, only the NSCF could differentiate them.

Campbell *et al*. [1] used the BioVid Heat Pain Database [5] with the aim to obtain meaningful features for pain recognition. They used the EMG (from the zygomaticus, corrugator, and trapezius muscles), ECG, and SCL signals from 85 people. Four classification problems were proposed: Baseline vs T1, Baseline vs T4, Baseline vs T1 vs T4, and Baseline vs T1 vs T2 vs T3 vs T4. Where T1 is the first pain level (pain threshold), T4 is the highest pain level (pain tolerance) and T2 and T3 are two linearly spaced values between T1 and T4. A total of 155 features were extracted from the signals and feature selection was performed using two approaches: Univariante Feature Selection (UFS) and Sequential Foward Selection (SFS). They adopted a one-hundred-epoch hold-out-and-k-fold cross-validation (CV) scheme using 75% of the data of each CV for training and the remaining 25% for testing. For the classification tasks, a set of SVMs with linear kernels in a one-against-one strategy was used. The best results were obtained using SFS with accuracies of 80.3%, 90.3%, 70.3% and 41.4% for each problem, respectively.

3 Protocol

The protocol implemented in this study is similar to the one implemented by Treister *et al*. [3]. Figure 1 summarizes the whole protocol.

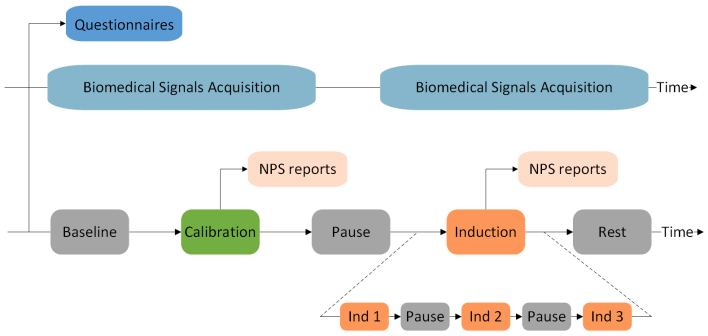

Figure 1: Scheme of the protocol implemented.

First, the process was explained to the participants and they filled out several questionnaires for the evaluation of personality traits, stress, and anxiety. During the session, biomedical signals (ECG, EDA, and EMG from triceps and trapezius) were recorded using non-invasive equipment along a baseline period (5 minutes), during pain induction, and at rest (5 minutes after). The pain was induced at the dorsum of the non-dominant and the EDA electrodes were placed on the middle (positive) and ring

(negative) of the same hand.

Three levels of stimuli of heat temperature were calibrated for each individual: low, medium, and high pain. The temperature was increased on a ramp of approximately 1°C for 10 seconds from 32°C to 49°C. The subject assessed the pain felt every 10 seconds using the 0-10 NPS. The average temperatures closest to the values of 3, 6 and 9 were calculated, corresponding to the three pain levels. It is important to refer that the process would stop if the person reported feeling a lot of pain or as soon as the person had an assessment of 9.

During the protocol, the stimuli were applied by order of intensity. The temperature of the thermode was increased to the target temperature where it remained constant for 1 minute. During these 60 seconds, the participants reported their pain perception every 5 seconds using NPS. This process was repeated for each pain level.

This study was approved by the Ethics and Deontological Council of the University of Aveiro (CED-UA-28-CED/2022).

4 Physiological Data Analyses

The signals were divided into epochs according to the protocol (baseline, induction 1, 2 and 3 and rest).

The signals were processed using the Neurokit2[1] software. From the ECG, ultra-short HRV features, mean HR and several features concerning the peaks and waves of the signal were extracted, resulting in 39 features. From both EMG signals, the mean amplitude of the signals and of the activations, and the number of activations per minute (6 features) were computed. Regarding the EDA, the mean of both tonic and phasic components, the number of peaks of the phasic component, and its mean values of amplitude, height, recovery time, and rise time were also computed (7 features). To minimize inter-participant variability, the features were scaled by the ratio between those features extracted from each induction and the respective extracted from the baseline, for each participant.

In order to test if the features differed significantly among the three pain levels and painless epochs, statistical tests were performed among the features extracted from the three inductions and rest epochs.

First, the normality of all the scaled features was tested using Shapiro-Wilk test. The features that did not meet the assumption of normality were submitted to a non-parametric Friedman test. Those that were likely to follow a normal distribution were submitted to a repeated measures ANOVA test. Afterwards, in case of statistical significant difference among the levels of pain, post-hoc tests (Nemenyi and pairwise t-tests with Bonferroni correction) were performed to evaluate which levels were significantly different from each other.

5 Results and Discussion

Among the 52 features tested, 21 of them showed statistical differences between at least two epochs (18 from ECG and 3 from EDA). Figure 2 shows the p-values obtained by post-hoc tests for all the features that showed differences among epochs.

	Features	I1 VS R	I2 VS R	I3 VS R	I1 VS I2	I2 VS I3	I1 VS I3
ECG	HRV_RMSSD	0.17	<0.05	<0.05	1.00	1.00	1.00
	HRV_MeanNN	<0.05	0.13	0.90	0.90	0.20	0.08
	HRV_SDNN	<0.01	<0.01	<0.05	0.90	0.76	0.41
	HRV_SDSD	0.20	<0.05	<0.05	1.00	1.00	1.00
	HRV_CVNN	<0.01	<0.01	<0.05	0.90	0.90	0.88
	HRV_TINN	<0.01	<0.01	0.06	0.65	0.73	0.15
	HRV_HTI	<0.01	<0.01	<0.01	0.76	0.90	0.65
	HRV_HF	<0.01	<0.01	<0.01	0.90	0.82	0.76
	HRV_LFHF	<0.01	<0.01	<0.01	0.88	0.82	0.41
	HRV_LFn	<0.05	0.47	0.65	0.53	0.90	0.35
	HRV_HFn	<0.01	<0.01	<0.01	0.90	0.76	0.47
	HRV_SD1	0.20	<0.05	<0.05	1.00	1.00	1.00
	HRV_SD2	<0.01	<0.01	<0.05	0.90	0.65	0.35
	HRV_ApEn	<0.01	<0.01	<0.01	0.90	0.82	0.53
	Mean_HR	<0.05	0.20	0.90	0.90	0.20	<0.05
	P_dist	<0.05	0.13	0.90	0.90	0.35	0.13
	R_dist	<0.05	0.13	0.90	0.90	0.20	0.08
	S_dist	<0.05	0.16	0.90	0.90	0.29	0.10
EDA	Mean_SCL	<0.05	<0.01	<0.01	0.76	0.90	0.59
	N_Peaks/min	<0.01	<0.01	<0.01	0.18	0.59	0.85
	SCR_RecoveryTime	<0.01	<0.01	<0.01	0.90	0.90	0.90

Figure 2: Result of the post-hoc tests.

[1] https://neuropsychology.github.io/NeuroKit/ (Accessed 25 August 2023)

From the ECG signal, the features that show significant differences are mainly related to HRV or to the distance between consecutive peaks. From EDA, features that could differentiate between inductions and rest were the mean of the tonic component, the number of peaks per minute and the rise time of the phasic component.

None of the EMG features showed statistical differences, which may be due to the fact that during whole protocol, the participants had their non-dominant arm leaning on the table which limited their movements.

The results obtained are in agreement with the statement that distinguishing a painless state from a state of pain is easier than distinguishing between states of pain at different levels, supported by the related works [1, 3]. Only one feature (mean HR) could differentiate between two pain levels (low and high). All the other features differentiate between no pain and at least one pain level.

On the other hand, it was expected that the high-pain stimulus was more differentiated from the rest epoch than the low-pain stimulus, which did not happen. The low level was the first to be performed. Thus, anxiety may be a factor here. The participants could feel more stressed before performing the first induction, which could influence the physiological response. Moreover, although they may feel more pain at the highest level, they already underwent through two inductions. Table 1 presents a comparison to the related works.

Table 1: Comparison of results obtained with the related works.

Authors	Participants	Features	Results
Triester et al. [3]	55 participants (34 men) aged from 20 to 37 y.o.	HR and HRV (from ECG) PPG pulse amplitude NSCF and SCL (from EDA)	The 5 parameter differentiated between pain and no pain Low VS Medium: Low VS High: Medium VS High:
Campbell et al. [1]	85 participants (BioVid Database)	a total of 155 features (selected using UFS and SFS)	B vs T1: 79.4% and 80.3% B vs T4: 72.9% and 90.3% B vs T1 vs T4: 63.4% and 70.3% B vs T1 vs T2 vs T3 vs T4: 40.6% and 41.4% (accuracies using UFS and SFS, respectively)
Our work	39 participants (10 men) aged from 18 to 27 y.o.	a total of 52 features	21 features (18 from the ECG and 3 from the EDA) could differentiate between at least one level of pain and no pain. Features that performed better are mainly HRV and EDA features

Comparing our results to those presented by Treister *et al.* [3], the extracted features in common (Mean_HR, HRV_HF, N_Peaks/min and Mean_SCL) also differentiate between pain and all the pain levels, except for the mean of HR. However, the calibration process applied by the authors and the local where EDA was collected was different from ours and in our work we did not remove subjects with mismatches between pain reports during calibration and induction which can explain the disctint results found.

6 Conclusion and Future Research

In this work, the response to different pain levels induced by heat was analysed with improved methodologies face to the current state of the art.

From all the features extracted and analysed, 21 features obtained from ECG and EDA showed statistical differences between painful and painless epochs that, for the novelty, opens new frameworks on the field.

These results motivate further studies with regard to pain induced by heat stimulus. Future research should engage a greater number of participants from a larger sociodemographic pool, yielding a more extensive dataset, suitable for automated pain classification.

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