Preprints of the 19th World Congress
The International Federation of Automatic Control
Cape Town, South Africa. August 24-29, 2014

Physiological Signals Based Quantitative Evaluation Method of the Pain

Yaqi Chu†*. Xingang Zhao*. Jun Yao†
Yiwen Zhao*. Zhenwei Wu*

† College of Information Science and Engineering,
Shenyang Ligong University, Shenyang, Liaoning, 110159, China
(e-mail: chuyaqi@sia.cn)
(e-mail: yjuna@sina.com)
** State Key Laboratory of Robotics, Shenyang Institute of Automation (SIA),*
Chinese Academy of Sciences (CAS), Shenyang, Liaoning, 110016, China
(e-mail: {zhaoxingang, zhaoyiwen, wuzw}@sia.cn)

Abstract: Quantitative analysis of pain is extremely difficult, because it is a subjective and individual sensation caused by the potential or existing observable tissue injury. For individuals with major cognitive or communicative impairments, it is necessary to carry out an effective method to quantify pain without self-report. Focusing on using physiological signals of the human body to evaluate pain, this paper proposes a new quantitative evaluation method with multiple physiological information to recognize the intensity of pain, which is induced by electrical stimulation that can be measured. When different intensity electrical stimulation applying on the subject, three-channel biosensors (BVP, ECG, SC) were used to obtain blood volume pulse, electrocardiogram and skin conductance. Experiments show that the proposed method can estimate the intensity of stimulation, which means that it can give the objective and quantitative evaluation of the pain.

Keywords: quantitative analysis, pain intensity, physiological signals, electrical stimulation, self-report

1. INTRODUCTION

Pain is an unpleasant physiological reaction caused by the existing or potential tissue damage (Hudspith *et al*. 2006), usually accompanied by a complex change of pathology and physiology. The physical and mental health of patients is affected by pain. As one of the most common clinical symptoms, pain has been identified as one of the five vital signs, in company with the breath, pulse, blood pressure and body temperature. According the survey data of the World Heath Organization, more than 80% of patients will have a postoperative pain. Annually on a global scale, the International Association for the Study of Pain (IASP) vigorously launches its "Global Year Against Pain" to raise awareness of different aspects of pain and proposes "Pain relief is a basic human right" (Collett *et al*. 2007).

The mechanism of pain is not fully clear currently. It is generally believed that stimulus in free endings of thin myelinated and nonmyelinated fibers sends nociceptive information to pain receptors in the brain that detect noxious agents (Araujo and Miyahira, 2011), accordingly causing a feeling of pain. Meanwhile, the pain is influenced by both nociceptive transmission and central nerve system modulation; and psychological, social and other environmental factors (Frampton and Hughes-Webb, 2011). In medicine, pain is a symbol of danger signals and it often indicates the location of the lesion. What's more, the size and the development trend of pain are the barometers of human health. Therefore, how to timely and accurately record the patient's pain physiological information and accurately assess the size and development trend of pain are extremely important research value, both for further study of the physiological mechanism of the human nervous tissue, or for the treatment of patients and rehabilitation guidance.

1.1 The current study

Although pain is characterized as a symptom, it is a subjective personal experience or a perception (Frampton and Hughes-Webb, 2011). Early in life, people learned to express pain in a variety of ways based on the accumulation of experience in damage, such as language description, expression changes, etc. For decades, with the joint efforts of science researchers and professional clinicians in anesthesiology, psychology, pharmacology, many subjective measures of pain have been developed that produce consistent and reliable results when used properly and appropriately. In unidimensional pain scales, the three most commonly used methods are the categorical verbal rating scale (VRS), numerical pain rating scale (NPRS) and visual analogue scale (VAS) (Frampton and Hughes-Webb, 2011).They are all well validated in the cancer pain population (Caraceni *et al*. 2002). There are also multidimensional pain measurement tools that can be used to assess the wider pain experience, such as the McGill Pain Questionnaire (MPQ) and Brief Pain Inventory (Frampton and Hughes-Webb, 2011). Ransford et al. (1976) proposed the body surface integral method, also known as 45 body

areas rating scale (BARS-45), which is applied to those patients who cannot communicate normally. We can evaluate pain by calculating the percentage of pain in the total body surface area.

Although these studies are of practical significance，the studies aforementioned are based on the patients subjective experience, which are not objective and stable. Thus, the researchers have long sought to develop a physiology-based pain assessment that does not depend on patients' self-report (Shankar *et al*. 2009). Their efforts have focused on various physiological signals. Oliveira *et al*. (2012) evaluated the relation between pain, induced by electrical stimulation, and subjective perception and also with nociceptive flexion reflex represented by muscle activity (electromyography) detected on the femoral biceps after sural nerve stimulation. It is possible to objectively quantify pain based on the analysis of biopotentials. K. Ikeda (1995) developed an experimental system that can measure non-invasively various physiological data, which may be related to pain, under the condition of imposing reproducible pain stimulation. Their study is to establish the practical way of quantitative evaluation of pain sensation including the individual difference to some degree. A. B. Peskov *et al*. (2007) established a good correlation between electrical pulse amplitude and pain intensity determined according to visual pain scale. An Analgesia Nociception Index (ANI) based on heart rate variability analysis for real time pain measurement during a surgical procedure under general anaesthesia was described and developed (Rommel *et al*. 2012; Logier *et al*. 2010). Anaesthesiologists use this index as a complementary tool for optimized drug delivery. This indicator can also be as an index of emotion regulation processes and evaluate stress/anxiety in particular domain of incident management team training (Logier *et al*. 2010).

1.2 The importance of pain quantitative research

Quantitative assessment of pain is becoming the focus of study. However, current research has two aspects drawbacks. Firstly, a description of the pain level and the establishment of pain models are more dependent on subjective perceptions of patients. In addition, individuals with major cognitive or communicative impairments, such as intensive care unit patients, infants or older adults with dementia, may not be able to provide valid self-reports of pain (Li *et al*. 2008; Herr *et al*. 2006). For those individuals, it is very difficult to determine the presence or absence of pain. Secondly, while some physiological signals have shown statistically significant correlations with pain intensity, or with the existence of pain, generally it can only give qualitative information (Tristao *et al*. 2011; Rissacher *et al*. 2007; Bossart *et al*. 2007). Therefore, despite many researches, there is currently not an acceptable method for the quantitative assessment of pain in humans.

The work in this paper is novel in trying to classify physiological patterns for a set of seven states (including five kinds of pain states), by applying pattern recognition techniques beyond that of simple discriminants to the problem. We use new features, spatial transformations of features and combinations of these methods to recognize pain intensity. The contributions of this paper include not only a new ways for pattern analysis for pain states from physiology, but also the finding of significant classification rates from physiological patterns corresponding to seven states measured from a subject over many days. We also show that the day-to-day variations in physiological signals are large.

2. DATA ACQUISTION

Clinical methods for pain assessment, through the patient's subjective feelings and self-reports, can easily obtain data of pain that can be understood by nonspecialists. However, amateurs usually don't know what information is useful in physiological signal, especially information for pain analysis. Although people can recognize pain from physiology, it is not easy to do so by naturally observing 1D signal waveforms. On the other hand, it is tough to uniquely map physiological patterns onto specific pain intensity and that physiological signals are very sensitive to motion artefacts.

Although dealing with the recording devices can be tricky, a much difficult problem is that how to obtain the real truth data, or obtain data that truly corresponds to a particular pain state. In traditional study, the truth labels for the pain intensity were easily obtained by a subject's self-report. With physiology, little is known about how pain affects physiological signals, but the signals are indeed potentially more sincere expressions of the subject's pain state since they are rarely mediated by cognitive and social impacts. In our study, a certain stimuli which can induce pain were imposed on a subject. We recorded physiological signals corresponding to different stimulus intensity. We would like to label the data according to the stimulus intensity. These labels are considered to represent different pain states in our study.

2.1 Experimental scheme

In this paper, six subjects aged between 22-25 years old (SD=3.0) participated in the study. All participants were healthy without any history of medical, neurological or psychiatric illness and none reported having a chronic pain condition. Data were gathered with three sensors: 1) A BVP-Flex/Pro sensor measuring blood volume pulse placed against the palmar surface of the middle finger of the right hand with am elastic strap or a small length of adhesive tape. 2) An EKG-Flex/Pro sensor recording electrocardiograph signal, the two electrode method based on lead I. 3) A SC-Flex/Pro sensor measuring electro-dermal response from the abdomen of the index and ring fingers on the palm-side of the right hand. Skin Conductance, which as an indirect index of sympathetic activity, can real-time reflects physiological and psychological changes in the process of pain. The electrode strap must be fastened around a finger tightly enough so the electrode surface is in contact with the finger pad but not so tightly that it limits blood circulation. Sensors and sampling device were provided by the Thought Technology Company, chosen because these apparatuses are

small enough to attach to a portable computer and offers ten isolated channels for recording. The sampling frequency was set to 1024 HZ.

There are many ways that can induce pain, such as thermal or cold pain stimulation (Appelhans and Luecken, 2008), mechanically stimulated pain (Shankar *et al*. 2009; Matsunaga *et al*. 2005), electrically stimulated pain (Oliveria *et al*. 2012), etc. In this paper, electrical stimulation was used to induce pain. The source of stimuli was provided by a device of functional electrical stimulation named motionstim8, which can generate a current square wave with a certain pulse width. The amplitude and frequency of the current were adjustable. The value of the pulse amplitude can be confirmed as an objective index of pain intensity (Peskov *et al*. 2007). In the experiment, the stimulating frequency was set to 2 HZ. In order to avoid the stimulator impact on sensors, especially the ECG signal acquisition, the stimulating electrodes were placed at the position of the tibialis anterior muscle of the right leg, as far as possible away from the sensors.

To minimize motion artifacts, the participants were seated and relatively motionless in the whole process. Each day's session lasted around 30 minutes. In each session, seven states including five pain states were designed, namely: pre-stimulate (calm), 10mA-stimulate (stim10), 15mA-stimulate (stim15), 20mA-stimulate (stim20), 25mA-stimulate (stim25), 30mA-stimulate (stim30), post-stimulate (post). Each state we acquired 1 minute data, resulting in around 6 thousand samples per physiological signal. We continuously collected one week data from the same participant, establishing a 7th day's data set (Day1-7).

3. FEATURE EXTRACTION AND TRANSFORMATION

Since there was not yet a priori knowledge of physiological responses of pain, and not a good model to describe physiological signals, we proposed to choose commonly used statistics of physiological signals in time domain as the original features, such as the mean, median, variance, etc.

3.1 Feature set

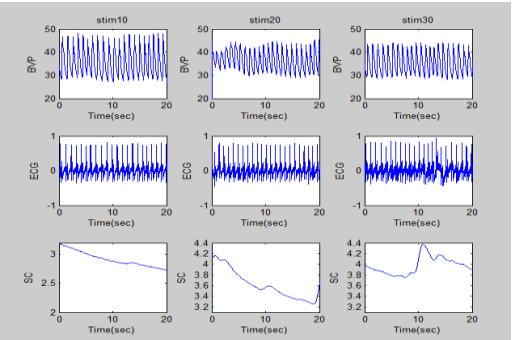

Figure.1. Examples of physiological signals measured from a person while he was in different pain state. From top to bottom: blood volume pulse (BVP), electrocardiogram (ECG), skin conductance (SC).

In addition to extract statistical features of original signals, we also extracted statistical features of the first difference of the raw signals. From the Figure 1, it can be seen that physiological signals were changed with the change of stimulus intensity. Hence, it is feasible to quantify pain intensity by extracting statistical features from physiological signals.

The statistical features can be calculated for each of signals as follows: Let the physiological signal (BVP, ECG, SC) from any one of the seven states be designated by X. Let X_i represent the value of the i th sample of the raw signal, where $i = 1, 2, ..., N$, with N represents the number of the samples. Following are formulas of used statistical features:

1). the means of the raw signals

$$\mu_X = \frac{1}{N}\sum_{i=1}^{N} X_i \tag{1}$$

2). the standard deviations of the raw signals

$$\sigma_X = \left(\frac{1}{N-1}\sum_{i=1}^{N}(X_i - \mu_X)^2\right)^{1/2} \tag{2}$$

3). the first differences of the raw signals

$$1d_X = X_{i+1} - X_i \tag{3}$$

4). the means of the absolute values of the first differences of the raw signals

$$\delta_X = \frac{1}{N-1}\sum_{i=1}^{N-1}|X_{i+1} - X_i| \tag{4}$$

5). the minimum ratio

$$\text{minRatio} = \frac{Min}{N} \tag{5}$$

Here, Min represents the minimum of the signal.

6). the maximum ratio

$$\text{maxRatio} = \frac{Max}{N} \tag{6}$$

Here, Max represents the maximum of the signal.

For obtaining the subtle changes of the signals in each state, we used a sliding window of 0.5 sec (the window length is 1 sec) to subdivide physiological signals. For 1 minute signals, we can obtain 119 samples. We do not expect to get all the features mentioned above or even to require such a huge number of features. In this paper, 34 features were extracted for three kinds of physiological signals. The first-order differential signal reflects the changing trend and speed of the raw signals. We eliminated some features extracted from the first-order differential signal of ECG and SC, which were almost the same values. Table 1 provides an overview of features, such as BVP1Diff-median represents the median value of the first differences of the blood volume pulse.

Table 1. Features used in this paper

BVP Feature	ECG Feature	SC Feature
BVP-mean	ECG-mean	SC-mean
BVP-std	ECG-std	SC-std
BVP-median	ECG-median	SC-median
BVP-min	ECG-min	SC-min
BVP-max	ECG-max	SC-max
BVP-range	ECG-range	SC-range
BVP-minRatio	ECG-minRatio	SC-minRatio
BVP-maxRatio	ECG-maxRatio	SC-maxRatio
BVP1Diff-mean		SC1Diff-mean
BVP1Diff-std		SC1Ddiff-std
BVP1Diff-median		
BVP1Diff-min		
BVP1Diff-max		
BVP1Diff-range		
BVP1Diff-minRatio		
BVP1Diff-maxRatio		

3.2 Feature reduction

Reducing the dimension of the feature space has two advantages. First of all, the computational costs are lowered and secondly the removal of noisy information may lead to a better classification results. Two general ways are Fisher Projection (FP) and Principle Component Analysis (PCA). PCA contains all the information of features and obtains a set of transformed features rather than a subset of the original features. However, a major disadvantage of PCA is that it does not include any class information. This approach can lead to lose important discriminating information.

Fisher Projection (FP) is a well-known dimensionality reduction method, which through a linear projection of the data into a fewer dimensional space for easier classification. FP uses class information to minimize scatter within classes and maximize scatter between classes. Due to the nature of the FP, the samples can only be projected to $c-1$ (or fewer) dimensions, supposing that original dimensions are more than $c-1$ dimensions, where c represents the number of classes. If the quality of some features is questionable, or if the number of training samples is not sufficient, some dimensions of the Fisher projection may be the result of noise rather than the result of differences between the classes. In this case, Fisher performs poorly in the testing samples. Alternatively, if the number of features n is smaller than the number of classes c, the Fisher projection is meaningful only up to at most $n-1$ dimensions. Therefore, the number of Fisher projection dimensions d_F is $1 \le d_F \le \min(c,n)-1$.

Consider the advantages of PCA and Fisher projection, a hybrid Fisher Projection with PCA (PCA-FP) method is proposed. We compared the results of classification between this hybrid method and Fisher projection without PCA. Note that the PCA method is used here as a preprocessor to reduce the dimensions of the features, and not as a classification method.

4. CLASSIFICATION

This section describes the classification algorithm and validation methods. We used linear discriminant analysis (LDA) as the classifier. The validation methods of normal-split or leave-one-out were used to evaluate the classifier. The normal-split method is a widely used validation method, which is to take 75% of the samples as the training set and the rest as the testing set. We also used the leave-one-out method for cross-validation because of the relatively small amount of samples and the high dimensional feature space. The specific algorithm was:

1). The sample points to be classified (the testing set only includes one sample for the leave-one-out method) are excluded from the sample set. The remaining sample set is used as the training set.

2). The Fisher projection matrix is calculated from only the training set. Then, both the training and testing set are projected down to the d dimensions by Fisher.

3). The sample in the d dimensional space is considered to be Gaussian. The respective means of the classes are estimated from the training set.

4). The Euclidean distance of the testing sample to the center of each class in d dimensional space is calculated.

5). The sample is then classified as coming from the class with the minimum distance.

5. RESULTS

This section presents some of the results obtained by applying the algorithm described above. First of all, we tried to just use the Fisher projection to recognize all seven states without PCA dimensional reduction. Figure 2 shows samples without PCA in Day1 projected onto the first three Fisher features.

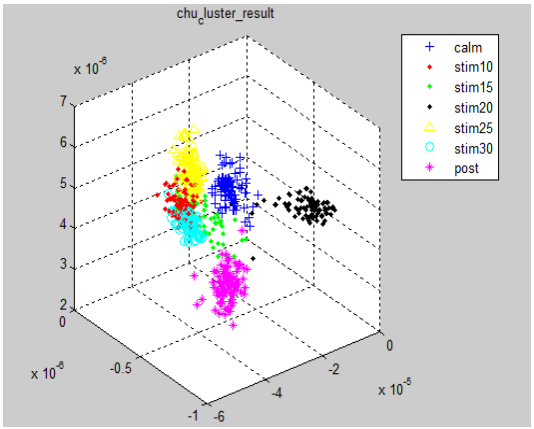

Figure. 2. An example feature set (Day1) without PCA projected onto the first three fisher features.

The overall classification accuracy for all seven states for Day1-7 for one person is shown in Table 2. Recognition rates of 70.95% to 83.91% were achieved by using leave-one-out method, which was better than 51.90% to 80.14% with normal-split method. Without PCA dimensional reduction, we can see that the classification accuracy was different from person to person in Table 3.

Table 2. The overall classification accuracy for all seven states for Day1-7

Day	Validation method	
	Normal-split	Leave-one-out
Day1	56.19%	79.47%
Day2	51.90%	80.91%
Day3	56.19%	74.43%
Day4	80.14%	83.91%
Day5	75.71%	70.95%
Day6	79.05%	77.31%
Day7	69.05%	72.75%

Table 3. The overall classification accuracy for six subjects

Subject	Validation method	
	Normal-split	Leave-one-out
Subject1	56.19%	79.47%
Subject2	75.71%	92.56%
Subject3	87.62%	87.03%
Subject4	80.48%	80.91%
Subject5	91.90%	92.32%
Subject6	72.07%	73.42%

Next, a hybrid Fisher Projection with PCA (PCA-FP) method was used to quantify the pain induced by the electrical stimuli in days. Figure 3 shows that the features with PCA from the same day clustered more closely than did features without PCA.

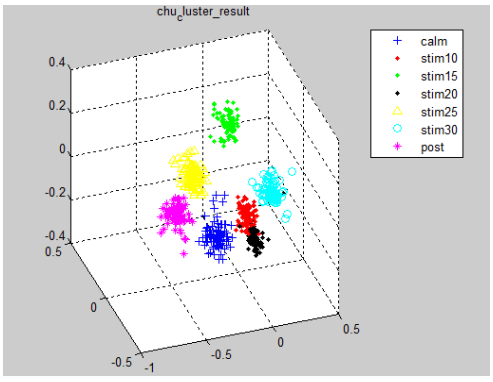

Figure. 3. An example feature set (Day1) with PCA projected onto the first three fisher features.

Similarly, we obtained the overall classification accuracy for Day1-7 with the same way. Table 4 gives the reviews of the result for Day1-7.The recognition rates of the two validation method are reached more than 90%. The results for six subjects are shown in Table 5 by using the same method.

Table 4. The overall classification results with the hybrid method for Day1-7

Day	Validation method	
	Normal-split	Leave-one-out
Day1	99.52%	99.76%
Day2	99.52%	99.28%
Day3	99.05%	99.28%
Day4	100%	99.88%
Day5	100%	99.88%
Day6	100%	100%
Day7	98.01%	99.64%

Table 5. The overall classification results with the hybrid method for six subjects

Subject	Validation method	
	Normal-split	Leave-one-out
Subject1	99.52%	99.76%
Subject2	100%	99.40%
Subject3	99.05%	99.28%
Subject4	100%	99.76%
Subject5	99.72%	99.52%
Subject6	99.60%	100%

Furthermore, we also showed the day-to-day variations in physiological signals for one person. We used the hybrid method to train sample set composed of Day1-7. Samples of each day were treated as testing set. Table 6 gives the testing results for each day. In addition to the results for Day2 and Day5 were reached more 50%, other classification results were low. The day-to-day variations are large by using this algorithm.

These variations are likely due to three factors: 1) sensor interface influences, including hand washing, application of different amounts of alcohol, and slight changes in positioning of sensors; 2) variations that are perception and reception dependent, such as an inability to build up intense experience of pain after a few days; 3) variations that may be caused by sleep, temperature, and other factors. The first factor is controllable by using disposable electrodes and always having washing his hand in the same way before every experiment. However, we made an effort to place the sensors as similarly as possible from day to day. Despite all this, many sources of variation are intrinsic and cannot be eliminated in realistic long-term measuring applications. How to reduce variations is needed in the future research.

Table 6. The classification results for each day (Day1-7) with the hybrid method

	Day1	Day2	Day3	Day4	Day5	Day6	Day7
Accuracy	38.18%	55.34%	40.10%	24.25%	56.90%	22.21%	29.65%

6. CONCLUSIONS

In this paper, we proposed a new idea for physiology-based pain assessment. Physiological signals were acquired in seven different states and a hybrid Fisher Projection with PCA method has been tested. We used linear discriminant analysis as the pattern recognition method to quantify the intensity of pain. Recognition rates of about 70% were achieved for all seven states. By applying the hybrid method, the results could be improved up to 98%. Although the rates found here can only be claimed to apply to one subject, the methodology proposed in this article can be used for any one. We also found that this methodology was not good to handling variations from day to day. In the future work, we need to consider how to reduce or eliminate these variations and then set up a general quantitative standard for pain.

ACKNOWLEDGEMENTS

The authors would like to thank Lingguo Kong *et al*. for participating this experiment. This work is supported by the National Natural Science Foundation of China (Grants nos. 61273355, 61273356, and 61273155), the Foundation of State Key Laboratory of Robotics (Grant no. Z2013-06).

REFERENCES

Hudspith, M. J., Siddall, P. J., and Munglani, R. (2006). Physiology of pain. *HEMMINGS, HC; HOPKINS, M. Foundations of Anesthesia*, 2.

Collett, B. J., and Berkley, K. (2007). The IASP Global Year against pain in women. *Pain*, 132, S1-S2.

Frampton, C. L., and Hughes-Webb, P. (2011). The measurement of pain. *Clinical Oncology*, 23(6), 381-386.

Caraceni, A., Cherny, N., Fainsinger, R., Kaasa, S., Poulain, P., Radbruch, L., and De Conno, F. (2002). Pain measurement tools and methods in clinical research in palliative care: recommendations of an Expert Working Group of the European Association of Palliative Care. *Journal of pain and symptom management*, 23(3), 239-255.

Araujo, E., and Miyahira, S. A. (2011). Tridimensional fuzzy pain assessment. In *Fuzzy Systems (FUZZ), 2011 IEEE International Conference on* (pp. 1634-1639). IEEE.

Ransford, A. O., Cairns, D., and Mooney, V. (1976). The pain drawing as an aid to the psychologic evaluation of patients with low-back pain. *Spine*, 1(2), 127-134.

Shankar, K., Subbiah, B. V., and Jackson, D. (2009). An empirical approach for objective pain measurement using dermal and cardiac parameters. In *13th International Conference on Biomedical Engineering* (pp. 678-681). Springer Berlin Heidelberg.

Oliveira, M. I., Machado, A. R. P., Chagas, V. G. S., Granado, T. C., Pereira, A. A., and Andrade, A. O. (2012). On the use of evoked potentials for quantification of pain. In *EMBC, 2012 Annual International Conference of the IEEE* (pp. 1578-1581).

Ikeda, K. (1995). Quantitative evaluation of pain by analyzing non-invasively obtained physiological data with particular reference to joint healing with continuous passive motion. In *Engineering in Medicine and Biology Society, 1995 and 14th Conference of the Biomedical Engineering Society of India. An International Meeting, Proceedings of the First Regional Conference., IEEE* (pp. 3-25). IEEE.

Peskov, A. B., and Stuchebnikov, V. M. (2007). Objective Measurement of Pain Intensity by Electrostimulation of Biological Active Points. In *Medical Measurement and Applications, 2007. MEMEA'07. IEEE International Workshop on* (pp. 1-3). IEEE.

Rommel, D., Nandrino, J. L., Jeanne, M., and Logier, R. (2012). Heart rate variability analysis as an index of emotion regulation processes: Interest of the Analgesia Nociception Index (ANI). In *Engineering in Medicine and Biology Society (EMBC), 2012 Annual International Conference of the IEEE* (pp. 3432-3435). IEEE.

Logier, R., Jeanne, M., Dassonneville, A., Delecroix, M., and Tavernier, B. (2010). PhysioDoloris: a monitoring device for analgesia/nociception balance evaluation using heart rate variability analysis. In *EMBC, 2010 Annual International Conference of the IEEE* (pp. 1194-1197). IEEE.

Logier, R., Jounwaz, R., Vidal, R., and Jeanne, M. (2010). From pain to stress evaluation using Heart Rate Variability analysis: development of an evaluation platform. In *EMBC, 2010 Annual International Conference of the IEEE* (pp. 3852-3855). IEEE.

Li, D., Puntillo, K., and Miaskowski, C. (2008). A review of objective pain measures for use with critical care adult patients unable to self-report. *The journal of pain*, 9(1), 2-10.

Herr, K., Bjoro, K., and Decker, S. (2006). Tools for assessment of pain in nonverbal older adults with dementia: a state-of-the-science review. *Journal of pain and symptom management*, 31(2), 170-192.

de Jesus, J. A. L., Tristao, R. M., Storm, H., da Rocha, A. F., and Campos, D. (2011). Heart rate, oxygen saturation, and skin conductance: A comparison study of acute pain in Brazilian newborns. In *Engineering in Medicine and Biology Society, EMBC, 2011 Annual International Conference of the IEEE* (pp. 1875-1879). IEEE.

Rissacher, D., Dowman, R., and Schuckers, S. A. C. (2007). Identifying frequency-domain features for an EEG-based pain measurement system. In *Bioengineering Conference, 2007. NEBC'07. IEEE 33rd Annual Northeast* (pp. 114-115). IEEE.

Bossart, P., Fosnocht, D., and Swanson, E. (2007). Changes in heart rate do not correlate with changes in pain intensity in emergency department patients. *The Journal of emergency medicine*, 32(1), 19-22.

Appelhans, B. M., and Luecken, L. J. (2008). Heart rate variability and pain: associations of two interrelated homeostatic processes. *Biological psychology*, 77(2), 174-182.

Matsunaga, N., Kuroki, A., and Kawaji, S. (2005). Superficial pain model using ANNs and its application to robot control. In *Advanced Intelligent Mechatronics. Proceedings, IEEE/ASME International Conference on* (pp. 664-669). IEEE.