Ultra-Short-Term Analysis of Heart Rate Variability for Real-time Acute Pain Monitoring with Wearable Electronics

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***Abstract*—In medical care, it is essential to assess and manage acute painful conditions adequately. Heart rate variability (HRV) analysis is based on the acquisition of electrocardiogram (ECG), which is available from both patient monitor and wearable device. As HRV analysis can reflect autonomic nervous system activity which is unconsciously regulated, HRV analysis in ultra-short-term is getting attention in indicating the reaction due to acute pain. Different HRV features in different window lengths are involved in pain monitoring studies as a signal index or part of a multi-parameter model. In this work, seven HRV features and median heart rate (HR) in ultra-short-term are evaluated for their competence in indicating experimental acute pain. Also, the choice of time window length in HRV analysis and its relation with pain detection are discussed. The results of the normalized HRV analysis from healthy volunteers show that the changes of lnRMSSD, pNN20 and median HR associated with the intensity of experimental electrical pain; and in the tests with experimental thermal pain, lnLF and ln(LF/HF) changed along with pain intensity. The fusion of the HRV features could tell pain from no pain. With either experimental pain stimulation, optimal time window length was observed around or larger than 40 seconds with better correlation analysis result and HRV feature fusion performance.**

***Keywords*— Heart rate variability, pain assessment, wearable device, experimental pain.**

I. Introduction

Pain assessment, as one of the critical points in pain management, relates closely to the quality of care in hospital and quality of life. Pain is common with a large population of people suffering from it. One in every four Americans was reported suffering from pain that lasts longer than 24 hours and a lot more suffered from acute pain in the year of 2006 [1]. Similarly, by the end of May in 2015, between one-third and one-half of the population in the UK were affected by chronic pain where pain lasts longer than three months. In addition, the proportion is likely to increase because of population aging [2]. Undertreatment of pain can lead to adverse consequences physiologically, psychologically and financially. For example, poorly management of acute pain may cause serious complications and progress to chronic pain; also, under-treated chronic pain influences daily activities and lowers the quality of life [3].

In pain assessment, pain intensity assessment is essential for pain management intervention and its evaluation. Patients are guided by caregivers to describe their pain intensities on a scale from 0 to 10, where 0 represents no pain, and 10 denotes the worst pain imaginable. Such self-report method is considered the " gold standard " as pain is believed to be a highly subjective experience, whereas it is impossible to obtain self-report in uncommunicatable situations from sedated or delirious patients for instance. In these situations, behavioral indicators of pain are observed by the nurse as an alternative way. No matter use which assessment tool, timely reassessment of pain by inquiry or observation is needed to assess treatment efficacy, but it barely can be real-time especially for acute pain. Furthermore, these tools rely heavily on nurses, their knowledge, interviewing techniques and physical assessment skill [4]. Therefore, an automatic pain intensity assessment tool is needed for real-time and continuous pain monitoring.

One potential approach towards automatic pain assessment is the fusion of physiological parameters, as multi-parameter analysis is superior to any individual physiological parameter [5]–[8]. Automatic pain assessment with physiological parameters has the advantage of leveraging wearable devices. With wearable devices, human physiological parameters are measurable and recordable even in everyday life. Wearable devices provide the foundation of health monitoring especially when integrated into an Internet-of-things system which enables wearable devices network with mobile devices, fog [9], as well as cloud servers. Such system may support various real-time health monitoring services by continuously processing and analyzing data from wearable devices.

Among the physiological signals available in wearable devices, signals that influenced by sympathetic tone are considered useful to indicate the perception of pain, and electrocardiogram (ECG) is one of them. From ECG record, heart rate (HR) and heart rate variability (HRV) can be derived to index sympathetic and parasympathetic nervous system activity when internal body functions are involuntarily regulated. HR, as one of the vital signs, is the most frequently observed physiological signal in pain studies. While HRV features measuring the variation time interval between heartbeats with different methods are observed individually and selectively in

some pain studies.

Therefore, HRV features in several categories are examined in this paper with their intercorrelation and correlation with pain for future physiological data fusion in pain detection or pain intensity assessment, serving as a reference in HRV features selection. In addition, HRV analysis in ultra-short-term is performed in this study instead of classical short-term in 5-minute windows and long-term in 24-hour time windows to address timely assessment and reassessment of acute pain.

In the rest of paper, HRV analysis methods and their relations with pain are introduced in Section II. Section III presents the study protocol designed for this study, where 1-lead ECG was recorded with a wearable strap around chest from thirty healthy volunteers under two experimental pain stimuli. Signal processing and data analysis methods are also presented in Section III. The following Section IV reveals the observations in HRV features as well as classification performance with selected HRV features. In the end, Section V concludes and discusses the study.

II. HRV Analysis in Pain Studies

Extracting HRV features from ECG starts with QRS detection. Only inter-beat intervals between adjacent normal R peaks are kept for HRV analysis. Those normal inter-beat intervals are usually referred as NN intervals in the literature. HRV features are measured over a period, typically in short-term over 5 minutes or in long-term over 24 hours. However, some HRV features in less than 1 minute as ultra-short-term analysis are also adopted, but in tracing acute psychological and physiological changes [10]–[12]. Within each time window, HRV features are calculated with numerous methods falling in three categories and they are i) time domain analysis, ii) frequency domain analysis and iii) nonlinear analysis [13].

HRV features in the time domain are statistically calculated from the interval lengths within each time window. Some common short-term time domain HRV features are:

- AVNN: average of NN intervals
- SDNN: standard deviation of NN intervals
- RMSSD: root mean square of differences between adjacent NN intervals
- pNNx: percentage of differences between adjacent NN intervals that are greater than x milliseconds;

HRV features in the frequency domain analysis are extracted from the spectrum of NN intervals in the corresponding time axis. To get the power spectrum with fast Fourier transform, the interval sequence can be evenly re-sampled. Alternatively, Lomb-Scargle periodogram [14] can be used directly to unevenly sampled data. Some common short-term frequency domain HRV features are:

- LF: low-frequency component, total spectral power between 0.01 and 0.15 Hz
- HF: high-frequency component, total spectral power between 0.15 and 0.04 Hz
- LF/HF: ratio of low to high-frequency power

where LF and HF are considered to index sympathetic and parasympathetic activity, respectively [10], [15]. Besides, correlations between SDNN and LF as well as RMSSD and HF were observed in healthy subjects, and the former was assumed as a surrogate for the latter [16]. The third category of HRV features uses nonlinear methods, which are considered more effective to describe the process generated by nonlinear biological systems. Among these methods, entropy in NN intervals is looked into in this study, where ApEn (approximate entropy) measures the disorder in NN intervals and SampEn (sample entropy) is similar to ApEn but better in studying the dynamics of human cardiovascular physiology [13].

HRV analysis in ultra-short-term has been applied as a path to measure pain in different types. For example, it was observed that standard deviation of Poincare plot, HR, and RMSSD in 1-minute windows were significantly different between eight chronic low back pain patients and eight healthy controls during movements [12]. Regarding acute pain, a finding was presented in Sesay *et al.* 's work [10], where LF and LF/HF in 30-second epochs significant increased among 120 patients when pain intensity was larger than 3 (numeric rating scale) after minor spinal surgery, but no significant change was found in HF. HF in every 1 minute was involved in [5] to monitor the clinical pain level with multi-parameter regression method.

Relatively, more studies were carried out with experimentally induced acute pain such as thermal pain or electrical pain. By reviewing the studies on HRV features in experimentally induced pain, LF was concluded to be valuable in response to pain induction, whose increase indicated an increase in sympathetic-baroreflex activity [15]. Also, the decrease of HF was highlighted to index a decrease in vagal-parasympathetic activity. In addition to extracting HRV features, a signal processing approach was developed to recognize experimental pain [17]. However, current studies also show that individual HRV feature is not capable to differ pain intensities or the subgroups of pain intensities although HRV analysis has potential in indicating the presence of pain [10], [18].

In this study, tests with experimental pain were carried out on healthy volunteers. From the gathered ECG records, ultra-short-term HRV features in different lengths were extracted to check the correlations between each of them and the presence of pain and compare the result with the studies mentioned above. HRV features were then compared and selected for the fusion in pain detection. The performance of HRV features fusion was presented as receiver operating characteristic (ROC) curve of classification.

III. Methods

Fifteen male and fifteen female volunteers in healthy condition with an average age of 35 (SD = 8) and 33 (SD = 11.9) were included in data analysis. The exclusion criteria include chronic, acute somatic and mental illness. Besides, cases with regular medication taken two weeks before or during the study were avoided as well. This study was approved by the Ethics

Committee of the Hospital District of Southwest Finland. The study was designed as follows:

A. Two experimental pain stimuli

Two types of experimental pain were employed in the tests to stimulate two types of sensory receptor. Electrical pain stimulus was delivered to the fourth finger of one hand with a digital transcutaneous electrical nerve stimulation (TENS) device [19]. The device generated biphasic rectangular pulses with a width of 250 microseconds and a repeat frequency of 100 Hz to cause pain. The voltage of the pulse can be incremented and decremented between 0 and 50, where the peak to peak output voltage in full scale was 100 volts. The second pain stimulus was thermal pain delivered to inner forearm skin from a heating element with a diameter of 3 centimeters. The temperature of the element surface was controlled to increase approximately linearly from room temperature and up to 52 degrees centigrade to avoid skin burn injury.

Each experimental pain stimulus was applied to the right and left side respectively, and thereby four tests were carried out on each volunteer. The four tests were conducted successively in a random order. The following test proceeded only when the HR of the subject was observed returning to his or her baseline if there was any change.

B. Test process

The subject was guided to first settle down in an armchair for around 10 minutes. After that, one pain stimulus was applied to him or her as the start of one test. The process of each test and data definition are presented in Figure 1. From the start time at t_0, the intensity of pain stimulus increased with a speed of 1 TENS level every 3 seconds or 1°C every 3 to 5 seconds until the volunteer reported reaching his or her pain tolerance at t_2 and the pain stimulus was then removed. During this process, the volunteer could indicate his or her pain threshold at t_1 by pressing a button which activated a buzzer.

Data in the time period without pain stimulus was defined as *No pain*; data between t_0 and t_1 was defined as *Mild pain*, which was equivalent to pain intensity below 3 and 4 in visual analog scale [20]; data between t_1 and t_2 was defined as *Moderate/Severe pain*, where the corresponding pain intensity in visual analog scale was between 5 and 10.

C. ECG measurement

During the whole experiment, the volunteer was wearing the Zephyr® Bioharness 3 wearable sensor and sitting in an armchair. The device can capture 1-lead ECG from chest area at a sample rate of 250 Hz with 12-bit analog-to-digital resolution. Its Bluetooth connection with a laptop and PC-based software ensured real-time wireless data transmission and real-time waveform visualization. Raw ECG records were saved as files for off-line processing.

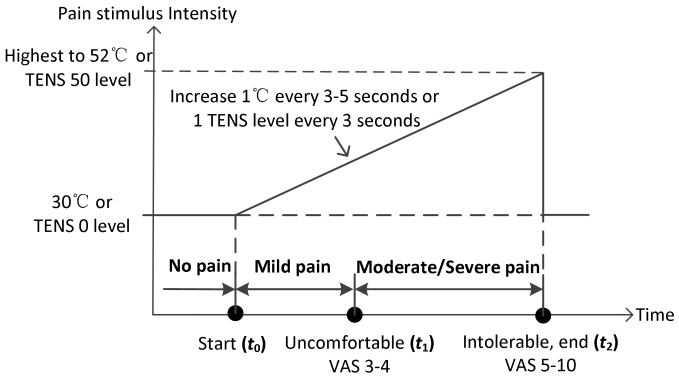

Fig. 1. Experimental study design

D. ECG signal processing

The aim of signal processing with ECG records in this study was to detect QRS wave in ECG waveform to extract NN intervals. Four steps were conducted in ECG processing:

1) 10-point moving average filter was applied to the whole record to remove the baseline wander in low frequency.
2) R peaks were detected with a threshold-based method, where the threshold was adaptively defined based on the maximum amplitude of the waveform. Moreover, for further precise R peak detection especially from P wave and T wave, minimum peak distance was added as a constraint according to normal heart rate range.
3) After the one round of detection, the detected R peaks were marked in the plotted ECG waveform, and they were manually validated in the third step. The distorted parts of the ECG record were abandoned, which are mostly at the beginning of the experiment due to device adjustment. Also in this step, several omitted R peaks were manually added.
4) Validated NN intervals were calculated from the positions of all detected R peaks. Meanwhile, all NN intervals were labeled as 1-*No pain*, 2-*Mild pain* and 3-*Moderate/Severe pain* respectively according to time stamps and the data definition in Figure 1.

E. HRV features extraction

Seven HRV features were evaluated including SDNN, RMSSD, pNNx, LF, HF, LF/HF and ApEn, which were from three categories as introduced in Section II. In the process of feature extraction, NN intervals were HR normalized by dividing by their average (AVNN) due to mathematical bias in NN intervals when referring different HRs [21]. This normalization is emphasized especially among people with different average HRs or during interventions that change HR [22]. The HR normalization narrows the gap between the big NN interval change at low heart rate and small NN interval change at high heart rate with the same amount of heart rate change. When extracting frequency domain features, Lomb-Scargle periodogram was applied as the spectral estimation

method. Besides these HRV features, median HR was also observed.

As the intensity of each pain stimulus increased progressively, HRV features in ultra-short time windows were extracted to track their dynamic change. HRV features in different time window lengths were first observed separately regarding their correlation with pain intensity. The window length was defined from 10 seconds to 60 seconds increasing in a step of 10 seconds. The HRV features were labeled as the most frequently occurring label among NN intervals in the time window. The sample sizes of each HRV feature in different time lengths are listed in Table I, where the sample size of 1-*No pain* was the largest and the sample size of 2-*Mild pain* in electrical pain tests were small due to the short transition from no pain to pain threshold.

TABLE I
SAMPLE SIZE OF HRV FEATURES IN DIFFERENT WINDOW LENGTH

Stimuli type	Label	HRV features window length					
		10 s	20 s	30 s	40 s	50 s	60 s
Electrical	1	1903	964	646	481	389	321
	2	89	44	21	16	11	11
	3	220	109	77	60	48	40
Thermal	1	2251	1125	747	564	452	375
	2	411	209	142	102	80	74
	3	244	113	77	58	47	31

To achieve normal distributions among the HRV features, SDNN, RMSSD, LF, HF and LF/HF were logarithmically transformed with natural logarithm [18]. Therefore, they are denoted as lnSDNN, lnRMSSD, lnLF, lnHF and ln(LF/HF) in Section IV. The signal processing and HRV analysis were implemented in Matlab.

IV. RESULTS

The root mean squares (RMSs) of HRV features in different time windows were first checked for its change with pain intensities. Several observations are obtained from Figure 2. Firstly, HRV features in electrical tests reacted more dramatically than those in thermal tests in general. Take median HR as an example. It changed from 70 bpm during *No Pain* to around 85 bpm during *Moderate/Severe pain* in electrical tests, while increased to around 75 bpm in thermal tests. This difference may validate that different pain-conducting nerve fibers were excited by these two different pain stimuli. Secondly, the relative relations of HRV features in different pain intensities may change with the length of the time window. In electrical tests, RMS of 10 s lnSDNN increased as pain intensity increase. However, it first went down and then went back to a close value when the time window length was 50 s. Similar pattern change can also be observed in ln(LF/HF) and median HR in both types of tests. Thirdly, pNN20 was responsive from *No Pain* to pain, but it tended to recover despite the ongoing pain stimulus. Last but not least, lnRMSSD, lnHF and median HR were found changing along with pain intensity in

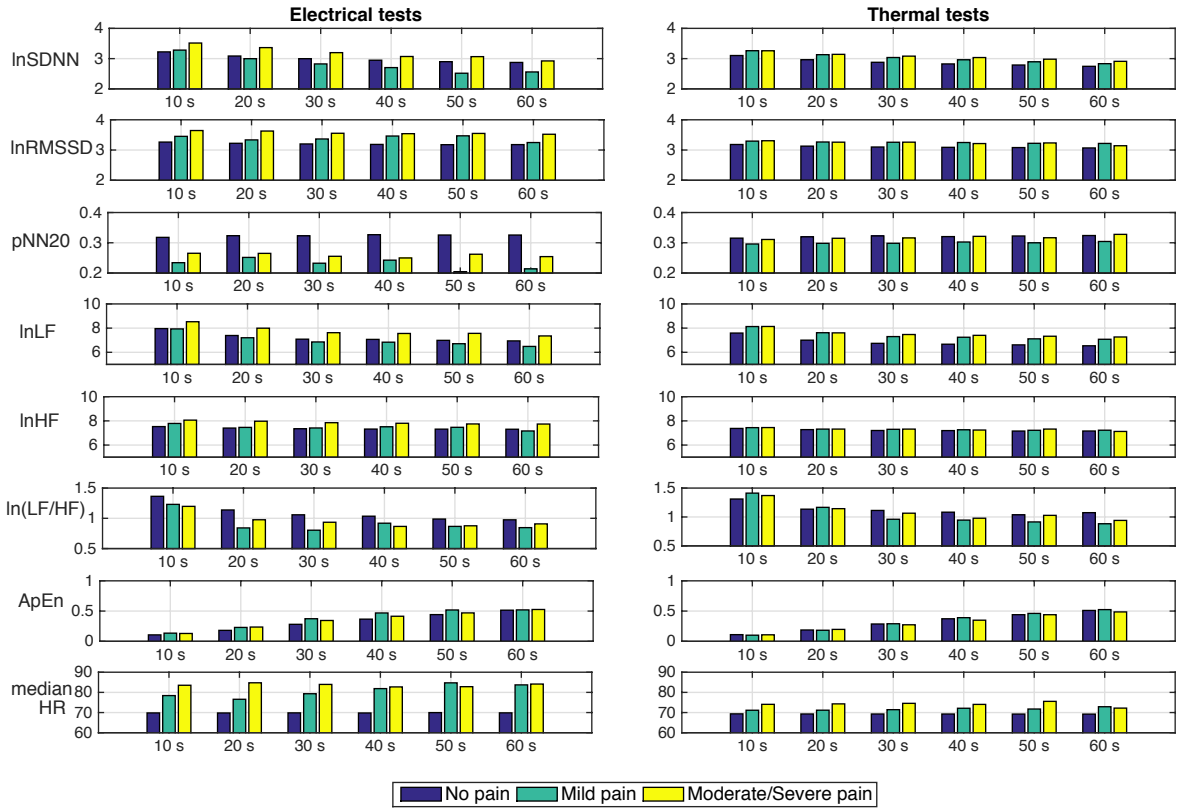

Fig. 2. Comparison of HRV features in different window lengths and different pain intensities. RMSs are compared in tests with the same pain stimulus.

TABLE II
PEARSON CORRELATION COEFFICIENT BETWEEN EACH HRV FEATURE AND PAIN INTENSITIES

HRV feature	Electrical pain, window length						Thermal pain, window length					
	10 s	20 s	30 s	40 s	50 s	60 s	10 s	20 s	30 s	40 s	50 s	60 s
lnSDNN	-0.1623*	-0.1504	-0.1021	NR**	NR	NR	**-0.1115**	**-0.1333**	**-0.1458**	**-0.1491**	**-0.1280**	**-0.1086**
lnRMSSD	**-0.2338*****	**-0.2545**	**-0.2400**	**-0.2617**	**-0.2766**	**-0.2334**	**-0.0897**	**-0.1044**	**-0.1266**	**-0.1123**	**-0.1175**	**-0.0953**
pNN20	**-0.1894**	**-0.2437**	**-0.2894**	**-0.3313**	**-0.3117**	**-0.3471**	NR	-0.0533	-0.0740	NR	NR	NR
lnLF	**-0.1094**	**-0.1309**	**-0.1309**	**-0.1268**	**-0.1528**	**-0.1036**	**-0.1354**	**-0.1785**	**-0.2080**	**-0.2192**	**-0.2119**	**-0.2280**
lnHF	**-0.1569**	**-0.1696**	**-0.1596**	**-0.1667**	**-0.1546**	**-0.1403**	NR	NR	NR	NR	NR	NR
ln(LF/HF)	NR	NR	NR	NR	NR	NR	**-0.1406**	**-0.1919**	**-0.2060**	**-0.2369**	**-0.2064**	**-0.2551**
ApEn	0.1355	0.1186	0.1522	0.1452	NR	NR	NR	NR	NR	NR	NR	NR
median HR	**0.3140**	**0.3363**	**0.3293**	**0.3226**	**0.3108**	**0.3495**	**0.1152**	**0.1198**	**0.1311**	**0.1327**	**0.1586**	**0.1106**
Absolute values sum****	1.0035	1.1350	1.1493	1.2090	1.2064	1.1738	0.5923	0.7278	0.8175	0.8502	0.8224	0.7976

* Underlined coefficient: statistically highly significant ($p < 0.001$)
** NR: not related. Hypothesis of no correlation: $p > 0.05$
*** Coefficient in bold: HRV features that were commonly correlated with pain intensities in all window lengths
**** lnRMSSD, pNN20, lnLF, lnHF and median HR in electrical tests; lnSDNN, lnRMSSD, lnLF, ln(LF/HF) and median HR in thermal tests.

electrical tests, while in thermal tests those were lnSDNN,lnLF and median HR.

The correlations between each HRV feature and the three pain categories in increasing pain intensities were then further looked into with Pearson correlation coefficient r, which are presented in Table II. The correlation whose p-value larger than 0.05 was considered as not related, and was marked as NR. The correlations that were statistically highly significant ($p< 0.001$) were highlighted with underlines. Additionally, for HRV features that were commonly correlated with pain intensities with all window lengths, their coefficients were highlighted with bold font. In electrical pain tests, HRV features including lnRMSSD, pNN20, lnLF, lnHF and median HR each showed small (r was between 0.1 and 0.29) to medium (r was between 0.3 and 0.49) correlation with the three pain categories. While there was a difference in the thermal tests, where lnSDNN, lnRMSSD, lnLF, lnLF/HF and median HR showed small correlation. The coefficients of these correlated HRV features were marked in bold font, and their absolute values in the same window length were summed. The highlighted HRV features were roughly consistent with the finding in Figure 2. pNN20 and lnLF in electrical tests as well as lnRMSSD and ln(LF/HF) in thermal tests were also found potentially useful from Table II in addition to the finding in RMS change from Figure 2. The sum of the highlighted HRV features showed that the overall correlation between HRV features and pain detection increased along with the increase of window length from 10 s to 40 s. After 40 s, the absolute values sum dropped slightly, but still better than that in shorter window length.

The relative relations among HRV features were next analyzed with Pearson correlation and principal component analysis (PCA). HRV features in 40 s window length were analyzed as a representative, and the PCA biplots in separate pain stimuli tests are presented in Figure 3. The similarity between lnSDNN and lnLF can be observed in Figure 3 (r=0.87 in electrical tests and 0.89 in thermal tests). A similar similarity was found between lnRMSSD and lnHF (r=0.90 in electrical tests and 0.94 in thermal tests). However, normalized lnSDNN and lnLF or lnRMSSD and lnHF in ultra-short-term performed inconsistently in the tests, as summarized from Figure 2 and Table II. Therefore, although there is strong linear correlation between lnSDNN and lnLF as well as between lnRMSSD and lnHF, the HRV analysis in time domain and in

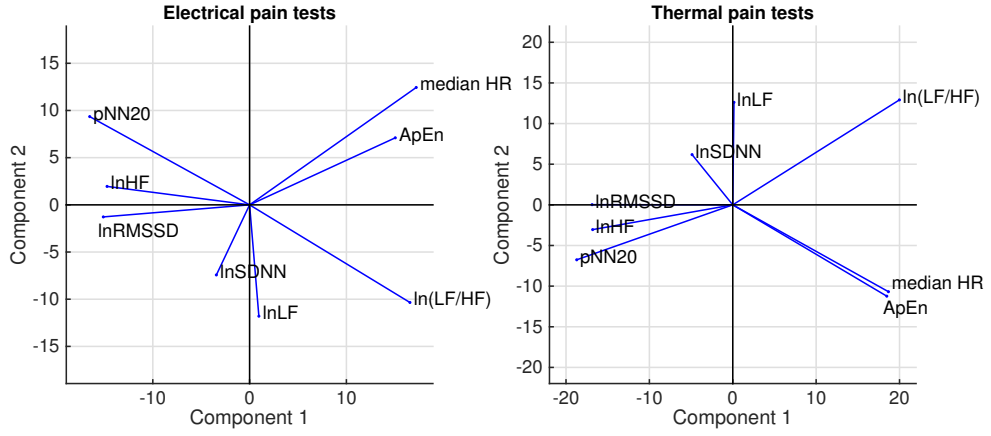

Fig. 3. Principal component analysis biplots of HRV features in 40 s time window

frequency domain are not equivalent.

Then, the HRV features highlighted in Table II were fused with support vector machine (SVM) classifier. Multi-class SVM classifier was first applied to the labeled HRV features in three categories, but the result was unsatisfactory where the overall classification accuracy in 10-fold cross validation was around 50%. Relatively, the binary classification results were more valuable in pain detection when rearranging the data labels as *No pain* and *Pain*. The binary classification results are shown in Figure 4 and Figure 5 with ROC curve and area under ROC curve (AUC). In accordance with prior observations, electrical pain stimulus was more predictable by HRV analysis than thermal pain stimulus because AUC with the former tests was higher than that with the latter tests in the same length of the time window. Moreover, either pain stimulus was better predicted with HRV features as the time window length increased.

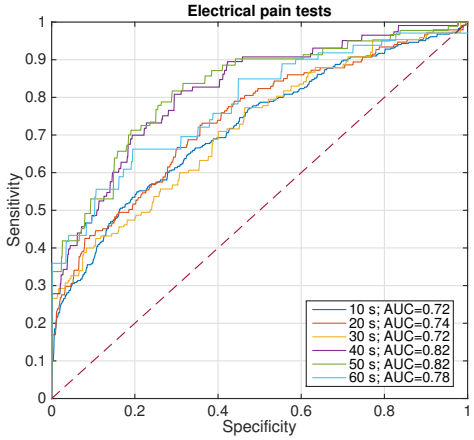

Fig. 4. Results of *No pain* and *Pain* classification in electrical pain tests

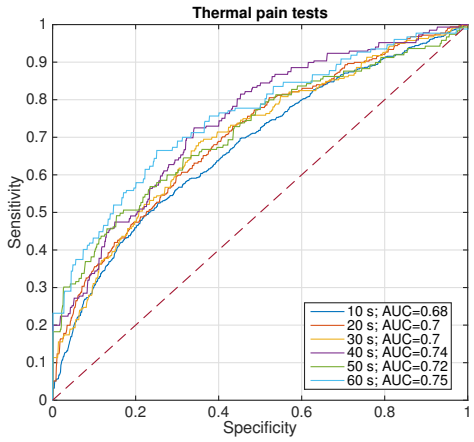

Fig. 5. Results of *No pain* and *Pain* classification in thermal pain tests

To observe how the combination of HRV features influences the classification performance, each possible combination of features in each window length was trained and tested by a binary SVM classifier. AUC was calculated as the performance measure. The results are presented as two heat maps shown in Figure 6. The total number of all combinations is 255. It includes the 8 cases of choosing 1 feature from the total 8 features (C_8^1), 28 cases of choosing 2 features (C_8^2), etc. The ROC curves in Figure 4 and 5 are from one case in the C_8^6 combinations. To highlight the combinations having the best performance, AUCs higher than 0.8 in electrical pain tests and AUCs higher than 0.75 in thermal pain tests are presented in red color. Figure 6 shows that 40 s and 50 s windows fit electrical pain tests better, while 60 s window fit thermal pain tests better. In terms of different feature combinations, the more features involved, the better chance to have good performance. The combination of lnSDNN, lnRMSSD and ln(LF/HF) reached similar good performance with the least number of features in both pain tests, where AUC(40, 40) = 0.8001 and AUC(40, 50) = 0.8066 in electrical pain tests, AUC(40, 60) = 0.7539 in thermal pain tests.

V. Discussion

Two experimental pain models in the skin are employed in this study. Thermal stimulation by slow heating that less than 1°C/s gives a preferential activation of C fibers, while electrical stimulation from TENS device activates non-nociceptive nerve fibers and also nociceptive nerve fibers directly bypassing nociceptors [23]. Human experimental pain models offer the possibility to explore the pain system under controlled settings and help understand pain mechanism [23], [24]. Usually, experimental pain tests on healthy volunteers are restricted in time with short pain stimulus in seconds or several minutes and the choice of time window length in HRV analysis is limited. For example, in BioVid database [6], thermal pain stimulus was maintained for 4 s, and it stopped for 8-12 s. In this case, 10 s time window was chosen for HRV analysis in time domain [25]. In this study, the time length of each test is determined by subject, so it varies among subjects and between pain stimuli. In electrical pain tests, *Mild pain* and *Moderate/Severe pain* took an average of 16 s and 37 s. In thermal pain tests, they took an average of 68 s and 50 s separately. With the same processing method, electrical pain is better identified from no pain than thermal pain when comparing Figure 4 and 5. In both types of tests, classification performance improves slightly with the increase of time window length in terms of AUC.

Independent of time window length in ultra-short-term analysis, there are some HRV features showing potentials in pain detection. Table II shows that lnRMSSD, pNN20, and median HR are correlated with electrical pain stimulus with high significance independent of time window length and lnLF and ln(LF/HF) are correlated with thermal pain stimulus with high significance. The decrease of RMSSD and/or HF is in line with the previous conclusion that it indexes a decrease in parasympathetic activity [15]. LF and LF/HF are observed decrease with the increase of thermal pain, which is contrary to previous studies where they increased [10], [15]. However, the consensus is reached that LF and LF/HF are

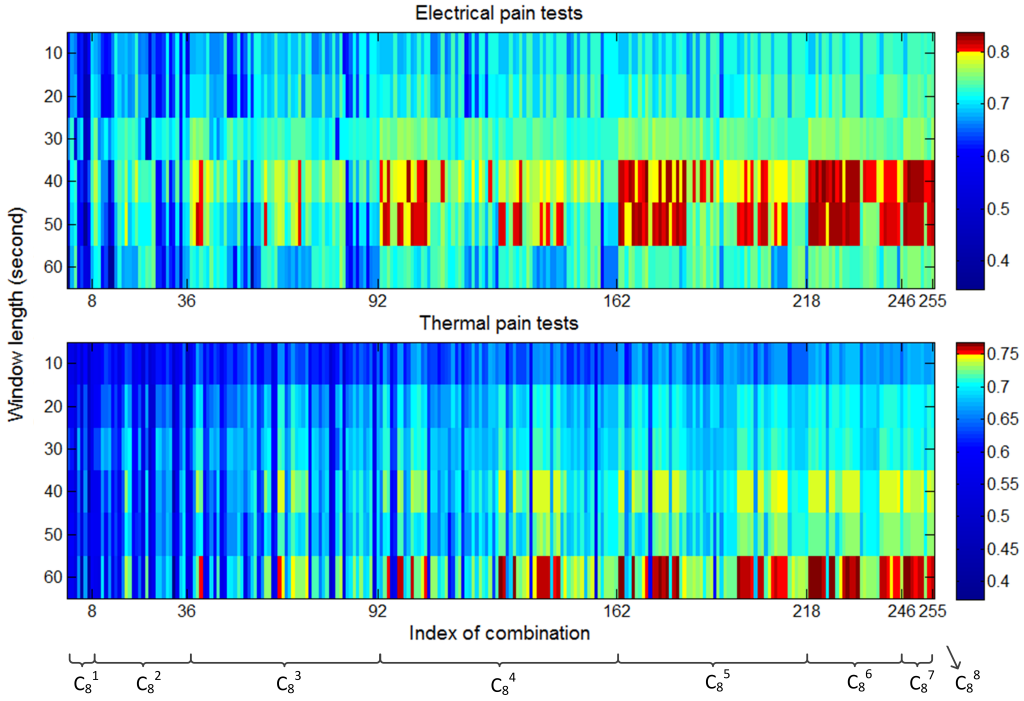

Fig. 6. AUCs of classifications with all possible feature combinations

potentially valuable HRV features in pain detection despite the disagreement in trend.

VI. Conclusion

In healthy volunteers, several HRV features in ultra-short-term within 1 minute changed accordingly with the intensity of experimental acute pain stimulation. In the tests with electrical stimulation activating nociceptive nerve fibers directly, lnRMSSD, pNN20 and median HR showed correlation higher than the others with the three pain categories. While in the test with thermal stimulation where C fibers were activated, lnLF and ln(LF/HF) showed a higher correlation with pain intensity than the other HRV features. These HRV features were small to medium linearly correlated to pain intensity. However, the multiple feature classification results did not show strong evidence in indicating pain intensity. Instead, they can potentially indicate the change from *No pain* to *Pain*. Furthermore, from a real-time point of view in acute pain monitoring, a better HRV feature fusion performance were achieved when time window length was around or larger than 40 s. The findings in this paper support ultra-short-term HRV features in acute pain monitoring and also provide a reference in HRV analysis method selection and time window length selection when less than 1 minute.

References

[1] National Institutes of Health, "NIH Fact Sheets-Pain Management." https://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=57.

[2] A. Fayaz, P. Croft, R. Langford, L. Donaldson, and G. Jones, "Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies," *BMJ open*, vol. 6, no. 6, p. e010364, 2016.

[3] P. H. Berry, C. Chapman, E. Covington, J. Dahl, J. Katz, C. Miaskowski, and M. McLean, "Pain: current understanding of assessment, management, and treatments," *National Pharmaceutical Council and the Joint Commission for the Accreditation of Healthcare Organizations, VA, USA*, p. b44, 2001.

[4] E. Wuhrman and M. F. Cooney, "Acute pain: Assessment and treatment," 2011. http://www.medscape.com/viewarticle/735034.

[5] N. Ben-Israel, M. Kliger, G. Zuckerman, Y. Katz, and R. Edry, "Monitoring the nociception level: a multi-parameter approach," *Journal of clinical monitoring and computing*, vol. 27, no. 6, pp. 659–668, 2013.

[6] S. Gruss, R. Treister, P. Werner, H. C. Traue, S. Crawcour, A. Andrade, and S. Walter, "Pain intensity recognition rates via biopotential feature patterns with support vector machines," *PloS one*, vol. 10, no. 10, p. e0140330, 2015.

[7] R. Treister, M. Kliger, G. Zuckerman, I. G. Aryeh, and E. Eisenberg, "Differentiating between heat pain intensities: the combined effect of multiple autonomic parameters," *PAIN*, vol. 153, no. 9, pp. 1807–1814, 2012.

[8] M. Huiku, K. Uutela, M. Van Gils, I. Korhonen, M. Kymäläinen, P. Meriläinen, M. Paloheimo, M. Rantanen, P. Takala, H. Viertiö-Oja, *et al.*, "Assessment of surgical stress during general anaesthesia," *British journal of anaesthesia*, vol. 98, no. 4, pp. 447–455, 2007.

[9] Y. Shi, G. Ding, H. Wang, H. E. Roman, and S. Lu, "The fog computing service for healthcare," in *International Symposium on Future Information and Communication Technologies for Ubiquitous HealthCare*, pp. 1–5, IEEE, 2015.

[10] M. Sesay, G. Robin, P. Tauzin-Fin, O. Sacko, E. Gimbert, J.-R. Vignes, D. Liguoro, and K. Nouette-Gaulain, "Responses of heart rate variability to acute pain after minor spinal surgery: optimal thresholds and correlation with the numeric rating scale," *Journal of neurosurgical anesthesiology*, vol. 27, no. 2, pp. 148–154, 2015.

[11] L. Salahuddin, J. Cho, M. G. Jeong, and D. Kim, "Ultra short term analysis of heart rate variability for monitoring mental stress in mobile settings," in *29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 4656–4659, IEEE, 2007.

[12] A. J. Hautala, J. Karppinen, and T. Seppänen, "Short-term assessment of autonomic nervous system as a potential tool to quantify pain experience," in *38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 2684–2687, IEEE, 2016.

[13] U. R. Acharya, K. P. Joseph, N. Kannathal, C. M. Lim, and J. S. Suri, "Heart rate variability: a review," *Medical and biological engineering and computing*, vol. 44, no. 12, pp. 1031–1051, 2006.

[14] P. Laguna, G. B. Moody, and R. G. Mark, "Power spectral density of unevenly sampled data by least-square analysis: performance and application to heart rate signals," *IEEE Transactions on Biomedical Engineering*, vol. 45, no. 6, pp. 698–715, 1998.

[15] J. Koenig, M. N. Jarczok, R. J. Ellis, T. Hillecke, and J. F. Thayer, "Heart rate variability and experimentally induced pain in healthy adults: A systematic review," *European Journal of Pain*, vol. 18, no. 3, pp. 301–314, 2014.

[16] H.-M. Wang and S.-C. Huang, "SDNN/RMSSD as a surrogate for LF/HF: a revised investigation," *Modelling and Simulation in Engineering*, vol. 2012, p. 16, 2012.

[17] S. Tejman-Yarden, O. Levi, A. Beizerov, Y. Parmet, T. Nguyen, M. Saunders, Z. Rudich, J. C. Perry, D. G. Baker, and T. Moeller-Bertram, "Heart rate analysis by sparse representation for acute pain detection," *Medical & biological engineering & computing*, vol. 54, no. 4, pp. 595–606, 2016.

[18] J. J. Meeuse, M. S. Löwik, S. A. Löwik, E. Aarden, A. M. Roon, R. O. Gans, M. Wijhe, J. D. Lefrandt, and A. K. Reyners, "Heart rate variability parameters do not correlate with pain intensity in healthy volunteers," *Pain Medicine*, vol. 14, no. 8, pp. 1192–1201, 2013.

[19] "Sanitas SEM43 Digital EMS/TENS." http://www.sanitas-online.de/web/_dokumente/GAs/therapie/752.907-0212_SEM43.pdf.

[20] G. A. Hawker, S. Mian, T. Kendzerska, and M. French, "Measures of adult pain: Visual analog scale for pain (vas pain), numeric rating scale for pain (nrs pain), mcgill pain questionnaire (mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap)," *Arthritis care & research*, vol. 63, no. S11, pp. S240–S252, 2011.

[21] J. Sacha, "Why should one normalize heart rate variability with respect to average heart rate," *Frontiers in physiology*, vol. 4, 2013.

[22] G. E. Billman, H. V. Huikuri, J. Sacha, and K. Trimmel, "An introduction to heart rate variability: methodological considerations and clinical applications," *Heart Rate Variability: Clinical Applications and Interaction between HRV and Heart Rate*, p. 6, 2015.

[23] A. E. Olesen, T. Andresen, C. Staahl, and A. M. Drewes, "Human experimental pain models for assessing the therapeutic efficacy of analgesic drugs," *Pharmacological reviews*, vol. 64, no. 3, pp. 722–779, 2012.

[24] C. Staahl and A. M. Drewes, "Experimental human pain models: a review of standardised methods for preclinical testing of analgesics," *Basic & clinical pharmacology & toxicology*, vol. 95, no. 3, pp. 97–111, 2004.

[25] F. M. Lima, S. Walter, S. Schach, H. C. Traue, and A. O. Andrade, "Pain-related heart rate variability responses in the context of experimental pain stimulation," in *IX Simpsio de Engenharia Biomdica*, pp. 42–45, 2016.