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ORIGINAL ARTICLE

Heart rate analysis by sparse representation for acute pain detection

Shai Tejman-Yarden[1,3,10] · Ofer Levi[2] · Alex Beizerov[3] · Yisrael Parmet[2] · Tu Nguyen[4] · Michael Saunders[5] · Zvia Rudich[6] · James C. Perry[1] · Dewleen G. Baker[7,8] · Tobias Moeller-Bertram[9,8]

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Abstract Objective pain assessment methods pose an advantage over the currently used subjective pain rating tools. Advanced signal processing methodologies, including the wavelet transform (WT) and the orthogonal matching pursuit algorithm (OMP), were developed in the past two decades. The aim of this study was to apply and compare these time-specific methods to heart rate samples of healthy subjects for acute pain detection. Fifteen adult volunteers participated in a study conducted in the pain clinic at a single center. Each subject's heart rate was sampled for 5-min baseline, followed by a cold pressor test (CPT). Analysis was done by the WT and the OMP algorithm with a Fourier/Wavelet dictionary separately. Data from 11 subjects were analyzed. Compared to baseline, The WT analysis showed a significant coefficients' density increase during the pain incline period ($p < 0.01$) and the entire CPT ($p < 0.01$), with significantly higher coefficient amplitudes. The OMP analysis showed a significant wavelet coefficients' density increase during pain incline and decline periods ($p < 0.01$, $p < 0.05$) and the entire CPT ($p < 0.001$), with suggestive higher amplitudes. Comparison of both methods showed that during the baseline there was a significant reduction in wavelet coefficient density using the OMP algorithm ($p < 0.001$). Analysis by the two-way ANOVA with repeated measures showed a significant proportional increase in wavelet coefficients during the incline period and the entire CPT using the OMP algorithm ($p < 0.01$). Both methods provided accurate and non-delayed detection of pain events. Statistical analysis proved the OMP to be by far more specific allowing the Fourier coefficients to represent the signal's basic harmonics and the wavelet coefficients to focus on the time-specific painful event. This is an initial study using OMP for pain detection; further studies need to prove the efficiency of this system in different settings.

Keywords Pain · Heart rate variability · Wavelet transform · Orthogonal matching pursuit algorithm

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1 Introduction

Objective pain assessments and measurements have long been a challenge as pain is a subjective sensation depending on physical and mental factors. Descriptive pain rating

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tools were developed in an attempt to quantify this experience. The one-dimensional pain scales, such as the visual analog score (VAS), are routinely used today for rating pain as one of the patient's vital signs [8, 30]. Studies though show poor correlation between the pain intensity expressed by patients on self-assessment scales and their caregivers' assessments; the greater the intensity, the poorer the correlation [6, 12, 23, 29]. Thus, accurate recognition of acute pain would allow immediate and proper treatment for unresponsive patients during acute illness or under general anesthesia.

Physiological variables such as skin conductance [10, 13, 26] and heart rate measurements [10, 27] were studied but found to be unreliable markers of acute pain [5, 9, 14, 15]. A study by Sisto et al. [24] reported a neonatal pain detector using an acoustic analysis algorithm of crying to provide an objective estimate of neonatal pain. The heart rate itself was further studied by applying mathematical tools such as the heart rate variability (HRV) and other spectral analysis methods (SAM) like the Fourier transform [3, 4, 16, 20]. Extensive studies on adult and pediatric populations using SAM have not managed to produce a reliable, real-time pain detector [17, 21, 25]. This was probably due to the fact that the ECG and other biological signals are non-stationary, dynamic signals which consist of harmonic rhythms (like the breathing pattern known as sinus arrhythmia) and sharp changes, reflecting reflex and/or anticipated responses to internal and external stimuli [3, 4]. The SAM are suited for time-invariant signals consisting of pure periodic patterns, thus failing to detect at real-time point events, accompanied by sudden rhythm changes which are of our interest.

For acute events, the Wavelet transform (WT) could be better suited due to its properties of representing signals with a finite number of sudden short duration and time localized changes that differ from the baseline harmonics [1, 2, 11, 18]. Other methods using advanced digital signal processing methodologies, like the orthogonal matching pursuit (OMP) algorithm [19] and the basis pursuit algorithm [7, 22], merge several different analysis methods to create a so-called over-complete dictionary depicting the different elements of the signal so to find an optimal representation of the biological signal. Thus, using both the SAM for representing the harmonics of the signal and the WT for localizing the acute changes may serve as a solution for acute pain detection.

The heart rate is a readily available parameter in almost every monitored clinical setting. Though not specific, it reacts sharply to acute painful stimuli. The aim of this study was to assess the heart rate of healthy young adults during an acute painful event, a cold pressor test, by using the new mathematical algorithms which were developed during the past two decades. Our hypothesis was that the coefficients of the WT can be related to the acute painful stimulus and that heart rate analysis by the OMP algorithm with an over-complete Fourier and Wavelet dictionaries could even improve the detection. The two analysis methods, the WT and the OMP algorithm, were applied separately to the heart rate signal as objective tools for acute, time-related pain detectors and their performances were compared.

2 Methods

The study was approved by the Ethics Committee of the Soroka University Medical Center in Beer Sheva, Israel. The cold pressor test and ECG sampling were conducted in the Soroka University Medical Center Pain Clinic in Beer Sheva, Israel. Signal processing was performed later in the signal processing laboratory in the Faculty of Biomedical Engineering in Ben Gurion University in Beer Sheva, Israel, in collaboration with the Faculty of Electrical Engineering in the University of California, San Diego.

2.1 Subjects

Fifteen healthy adult volunteers with no active medical disorders and no cardiac or neurological history signed informed consents before participation in the study. The participants' mean age was 28.1 $\pm$ 3.5 years (ten males and five females). All subjects were healthy with no current medical issues. Subjects with cardiovascular, neurological or other systemic problems were excluded from the study.

2.2 Study protocol

After signing an informed consent, each subject was connected to the ECG polygraph and sampled for 5 min in a quiet environment with minimal interference as baseline measurement. At the end of the baseline sampling, the subject was read the protocol again and was requested to dip his or hers dominant hand into a bath of icy water. Pain rating started immediately upon initiation of the cold pressor test, and the pain was rated using the VAS, for which the subject placed a mark on a scale from 0 to 10 to indicate the intensity of pain; 0 is labeled as "no pain", and 10 is labeled as "worst possible pain." Each subject performed the cold pressor test as long as he or she could endure it. Sampling was continued during the recovery time after the hand was taken out of the bath until no pain was reported. Subjects were able to end the test or the sampling at any time. During the entire study, the subject was seated and ice bucket was adjusted to the dominant hand.

2.3 The sampling system

ECG signals were recorded from three skin surface electrodes at a sampling rate of 1000 Hz using an "Atlas Researches LTD" polygraph connected by USB to a laptop. The ECG samples were recorded in real time on the designated laptop for analysis at a later time in the signal processing laboratory.

2.4 Analysis methods

This research studied the wavelet coefficients of the RR signal. The wavelet functions are well localized in time. In both methods (the WT and the OMP algorithm), the wavelet coefficients were analyzed as markers for acute pain and were correlated with the personal VAS reported by the subject. As mentioned above, the VAS was our golden standard for pain measurement. The two parameters that were correlated with the painful stimulus were the coefficients' occurrence density and coefficients' amplitudes. We provide a short description of both the WT and the OMP algorithm. An extensive description of both methods is available in references [1, 2, 18].

2.4.1 Wavelet transform (WT)

The WT correlates a given signal $f(x)$ with a special set of defined functions $\psi(t)$ called *wavelets*. The chosen function, such as the Haar or the Daubechies function [18], is used to generate the entire signal using simple dilations (scaling) and translations (shifts) of the chosen function across the time line. In contrast to the Fourier transform which expresses the signal as a sum of waves (sines and cosines), the WT expresses it as a sum of the scaled and timed wavelets $\psi(t)$. The definition of the wavelet function is

$$\psi_{a,b}(x) = \frac{1}{\sqrt{a}}\psi((x-b)/a) \quad a \in R^{+} \quad b \in R$$

where a and b are the scale and translation parameters, respectively. The definition of the WT of the signal $f(x)$ is

$$W_{a,b}f(x) = \int_{-\infty}^{=\infty} f(x)\frac{1}{\sqrt{a}}\psi((x-b)/a)\mathrm{d}x = \langle f(x), \psi_{a,b}(x)\rangle$$

The wavelet transform W can therefore be thought of as the cross correlation of the analyzed signal with a wavelet function that has been translated by value b and dilated by factor a.

2.4.2 The orthogonal matching pursuit algorithm

OMP generates an adaptive approximation of the signal using a greedy approach. It decomposes the signal by successive approximations into a linear expansion of waveforms that belong to a possibly redundant dictionary of functions (called atoms) [2]. These functions are selected to best represent the studied type of signal and its components. OMP is a greedy least squares procedure that chooses the dictionary vectors one at a time, thus gradually reconstructing the signal using a set number of coefficients, each added gradually from the selected dictionaries (or transforms). Each coefficient is added layer by layer to build the reconstructed signal as close as possible to the original. After each selection step, the entire set of chosen coefficients is updated to make the signal approximation orthogonal to the residual vector. The residual norm is thereby minimized.

This study used OMP with a dictionary containing the Fourier and wavelet transforms, as their combination gives the unique ability to discriminate between underlined harmonics and acute time-related events. The algorithm decides which specific, most correlative coefficient to utilize from the combined Fourier–Wavelet dictionaries at each iteration as it rebuilds the signal. The optimization problem that OMP algorithm solves approximately can be stated as

$$\begin{aligned} &\min \|x\|_0 + \lambda\|r\|_2^2 \\ &s.t. : [A_1|A_2]x + r = b \end{aligned} \tag{1}$$

where b is the given signal, A_1 and A_2 are matrices that correspond to the Fourier and Wavelet bases, x is the representation of b using the given over-complete dictionary and r is the residual vector. $\|x\|_0$ is the number of nonzero entries in x, and λ is a sensitivity parameter. Since the size of b is n and x is $2n$ long, the linear system $[A_1|A_2]x = b$ is under-determined and has multiple solutions. The solution of problem (1) finds a sparse representation of the signal b using the over-complete Fourier–Wavelet dictionaries and at the same time keeps the residuals small. The λ parameter penalizes the size of the residuals, so when λ is large, it is expected that the optimal solution will have relatively small residuals, and when λ is small, the residuals might be relatively large.

At step $k = 1$, a single vector from the Fourier and Wavelet dictionaries that has the highest correlation with b is chosen by solving the following problem:

$$\min_{v}\left(\min_{c}\|b - cv\|_2\right) \tag{2}$$

where v is a vector of the matrix $[A_1|A_2]$ and $c \in R$ (real number). Let $\hat{b}_1$ be the resulting best approximation of b at the first step, and let $e_1 = b - \hat{b}_1$ be the error after that first step. Similarly, let $\hat{b}_k$ be the resulting best approximation at the kth step of b and let $e_k = b - \hat{b}_k$ be the associated

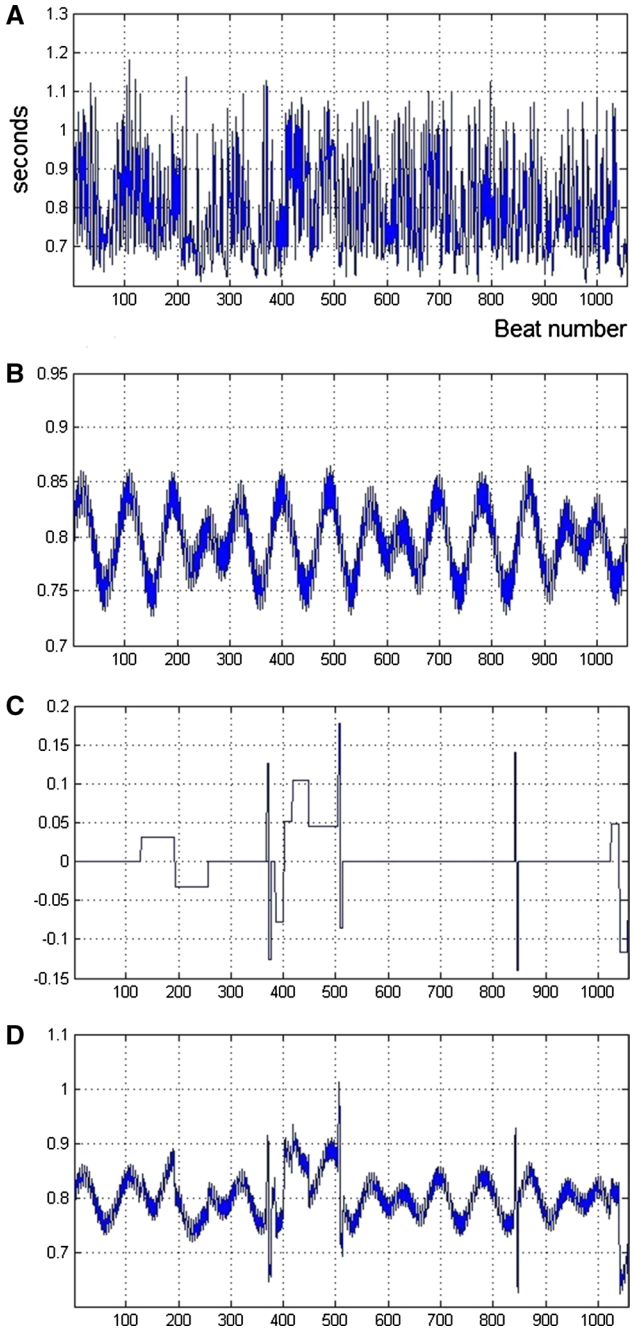

Fig. 1 Represents the OMP analysis method. Panel **a** shows the original RR signal, the tachogram of the subject. The *x-axis* represents the absolute number of the specific beat, and the *y-axis* represents the inter-beat time in seconds. Panel **b** represents the OMP RR signal partial reconstruction, Fourier components only. Panel **c** represents the OMP RR signal partial reconstruction, wavelet components only. Panel **d** represents the combined reconstruction using all components both Wavelet and Fourier

error. At the kth step, the next vector is determined by solving

$$\min_{v}\left(\min_{c}\|e_{k-1}-cv\|_2\right) \tag{3}$$

As mentioned, $\hat{b}_k$ is the approximation of b using the k chosen vectors that correlate with the minimal e_k. The entire set of k chosen coefficients is then updated so that cv is orthogonal to e_k. The algorithm terminates when the approximation error norm is below a tolerance.

Examples to this analysis method are given in Figs. 1 and 3. We can see in Figs. 1a and 3a the RR signals of the different subjects. Using an over-complete Fourier/Wavelet dictionary, the Fourier coefficients are presented in box b, the wavelet coefficients are presented in box c and the reconstructed signal in box d to give a sparse representation of the signal with the minimal coefficients needed. The separation into the two different analysis modalities allows us to evaluate the major harmonics (box b) and the major acute changes (box c) of the evaluated signal.

2.5 Signal preprocessing

Each ECG sample was reviewed separately to evaluate sampling noise and accurate *R* wave identification. In order for the results to be as clean and accurate as possible, short ECG segments that were noisy and could distort the analysis were cut out of the sample and disregarded (mainly due to motion artifacts). Each subject's sample was then analyzed by the MATLAB® program.

2.6 Signal processing

From the entire ECG sample (baseline and protocol), by identifying the tip of the *R* wave, an *R–R* signal was generated, named the tachogram. The *x*-axis represents the absolute number of the specific beat, and the *y*-axis represents the inter-beat time. Unlike the ECG signal, the tachogram can be regarded as relatively noise free as it takes into consideration only the heart rate, disregarding changes in *R* wave amplitude, ST and T changes, or baseline disturbances. A baseline tachogram of two subjects is presented in Figs. 1a and 3a.

The tachogram of each subjects' sample was analyzed twice: initially by the WT using the Haar wavelet and then by the OMP algorithm with an over-complete Fourier/Wavelet dictionary, also using the Haar wavelet. For both methods, each patient's signal was reconstructed using up to 40 coefficients. The OMP analysis method simultaneously extracted both local features, represented by the wavelet coefficients, and global harmonies, represented by the Fourier coefficients. It was shown experimentally that for proper delineation of the acute events, the local wavelet coefficients' amplitudes were multiplied by a 1.5–1.8 preference ratio parameter before choosing the mixed subset of high magnitude coefficients. The Haar wavelet transform used by the OMP algorithm was set to have the coarsest scale (approximation scale) as the seventh finest scale. In

this way, the overall seven scales correspond to time windows of 2 (finest scale) to 128 (coarsest scale used) beats. Coarser wavelet scales correspond to features spanned over 256 beats or more which were not considered local and therefore omitted. As for the Fourier coefficients, typically the chosen coefficients corresponded to frequencies of 0.015–0.25 Hz.

As the aim of this study was to detect acute pain using sparse representation of the RR signal, by using only 40 coefficients we limited ourselves to the minimal number of coefficients grossly needed for the signal's reconstruction and which maximally delineated the important events. Figures 1 and 3 represent the OMP analysis method applied on two different subjects' tachograms. Panels a represent the original tachogram of each subject, panels b and c represent the partial reconstructions from the Fourier part only and the Wavelet part only, respectively, and panels d represent the signal reconstruction from both the Fourier and the Wavelet coefficients. Figures 2a and 4a represent the partial reconstruction of the RR signal from the Wavelet coefficients only calculated by the OMP algorithm (similar to panel C in Figs. 1 and 3, respectively), but here the *x*-axis was translated from beats to time (this by adding up the inter-beat time). This was calculated to match the reconstructed RR signal with the experiments' protocols. Figures 2b and 4b represent the reconstruction of the RR signal using the 40 coefficients of the standard Wavelet transform. In these figures too, the *x*-axis was translated to time, to match the reconstructed RR signal with the protocol.

2.7 Data analysis

To evaluate the wavelet coefficients calculated by the two methods, each subject's sample was divided into four periods. The first period was the baseline, sampled in a quiet environment prior to the cold pressor test. The second period, "the pain incline period," included the anticipatory phase and the initial period of the cold pressor test. The anticipatory phase averaged 40 s in length and included the time during which the protocol was read to each subject again. The initial phase of the cold pressor test was the time in which the subject reported incremental pain via the VAS up to VAS 9 or 10. The third period was that of stable high pain levels (VAS 9 and 10). Finally, the last period was the pain decrement period, defined as the time after which the hand was removed out of the water and the VASs decreased as the pain resolved.

2.8 Statistical analysis

Statistical analysis was performed to correlate the wavelet coefficients' occurrence density at each period and amplitudes with the painful stimulus using the two methods. For each method, the wavelet coefficients' occurrence density at each time period of the cold pressor test was compared to the baseline period using the paired *t* test. Only the wavelets from the seven finest scales were regarded and counted, we did not evaluate each scale separately, giving different weigh to the different scales, rather we took equally into account the selected scales. The ANOVA on the log scale was used to compare the performances of the two analysis methods in the different periods of the protocol.

To analyze the amplitudes of the various stages, the LMM (linear mixed models) was applied on the log scale of the amplitude level. This was used due to the unbalanced structure of the data with the need to take into consideration the random effect of the different participants. We used the log transforms of the different levels to achieve model assumptions.

3 Results

Fifteen young adults participated in the study. The samples of four subjects were excluded. Two subjects withdrew as soon as they dipped their hand into the icy water and decided to stop the study, and two samples were not analyzed due to excessive motion artifacts or lead displacement throughout the entire study. These four samples' baseline and protocol ECG's were not analyzed and were not reviewed. Thus, only 11 subjects (nine males and two females) were included in the study analysis.

After calculating each subject's tachogram, the data were analyzed twice. The first analysis was done by the WT and the second by the OMP algorithm. Figures 1 and 2 represent the analysis performed on one subject's tachogram, and Figs. 3 and 4 represent the analysis performed on a different subject's tachogram. As described in the Methods section, Figs. 1 and 3 represent the OMP analysis process. Figures 2a and 4a represent the partial reconstruction of the RR signal from the Wavelet coefficients only calculated by the OMP algorithm, translated into seconds and correlated with the subject's protocol, and finally, Figs. 2b and 4b represent the RR signal reconstruction from the coefficients calculated by the standard WT, also translated into seconds.

Table 1 shows the distribution of the time-related wavelet coefficients and their density in the defined time periods as calculated by the two methods. Statistical analysis by a paired *t* test of the wavelet coefficients' density showed that during the baseline period there was a significant reduction in wavelet coefficients using the OMP analysis compared to the WT analysis ($p < 0.001$). The coefficients' density was 0.0433 ± 0.054 Hz (coefficients per second) using the WT and 0.0056 ± 0.0036 Hz using the OMP algorithm.

Analysis of the tachograms of the entire protocol by the standard WT showed that there was a significant increase in

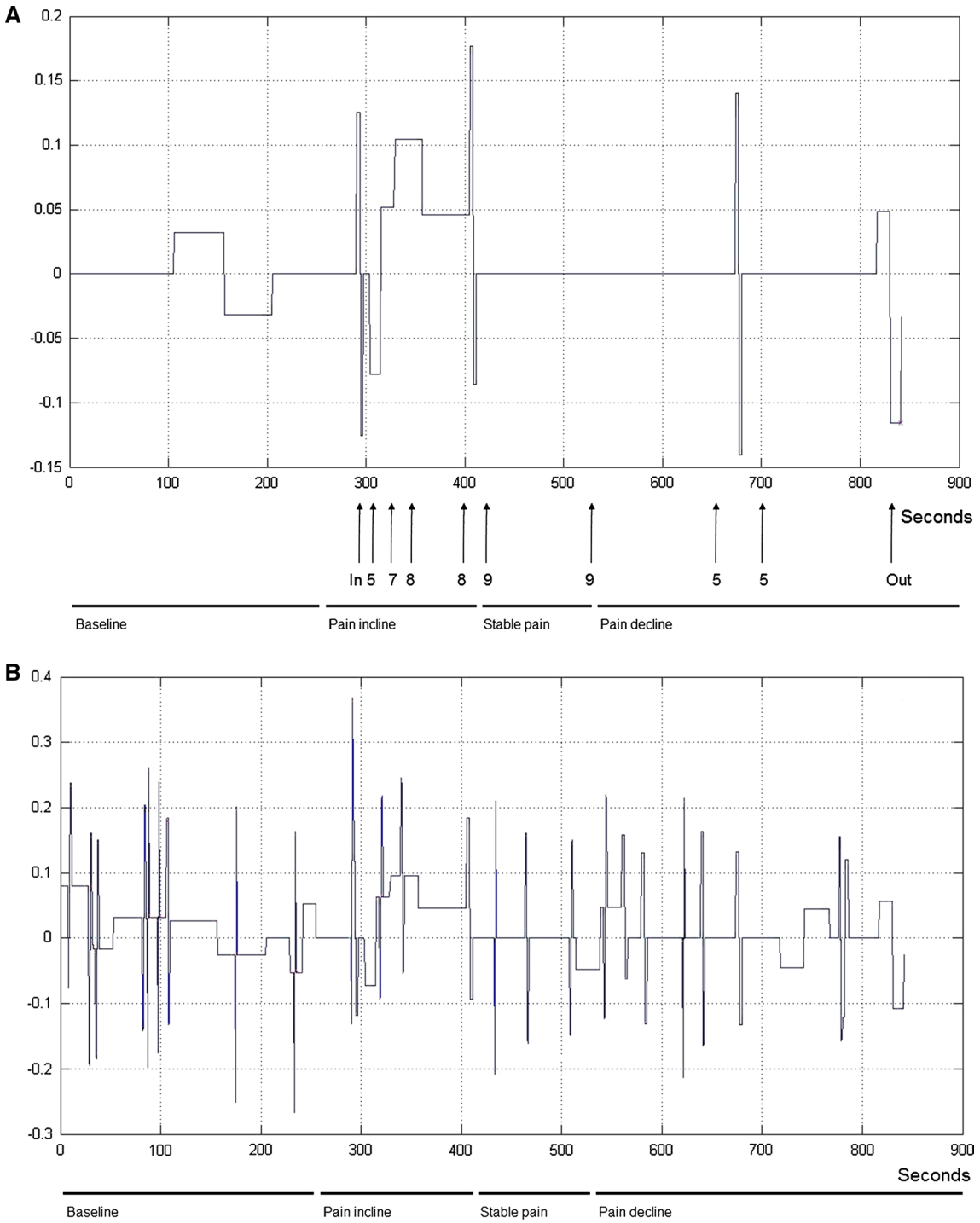

Fig. 2 Panel **a** represents the RR signal reconstruction from the wavelet coefficients only, obtained by the OMP algorithm in Fig. 1c. The *x-axis* is translated to seconds by adding the inter-beat time, and the partial reconstruction is compared to the subject's protocol indicated on the *x-axis*. Panel **b** represents the RR signal reconstruction from the wavelet coefficients obtained by **a** the standard wavelet transform. The *x-axis* as in panel **a** is translated to seconds for evaluation with the subject's protocol. Note that OMP analysis, shown in panel **a**, highlighted the pain-related transients, while WT, shown in panel **b**, provides a non-specific detection of transient episodes

the wavelet coefficient density during the pain incline period compared to the baseline period ($p < 0.01$). The baseline coefficients' density was 0.0433 ± 0.054 Hz, and the pain incline period coefficients' density was 0.063 ± 0.054 Hz. There were no statistically significant changes regarding the stable maximal pain period's coefficient densities compared

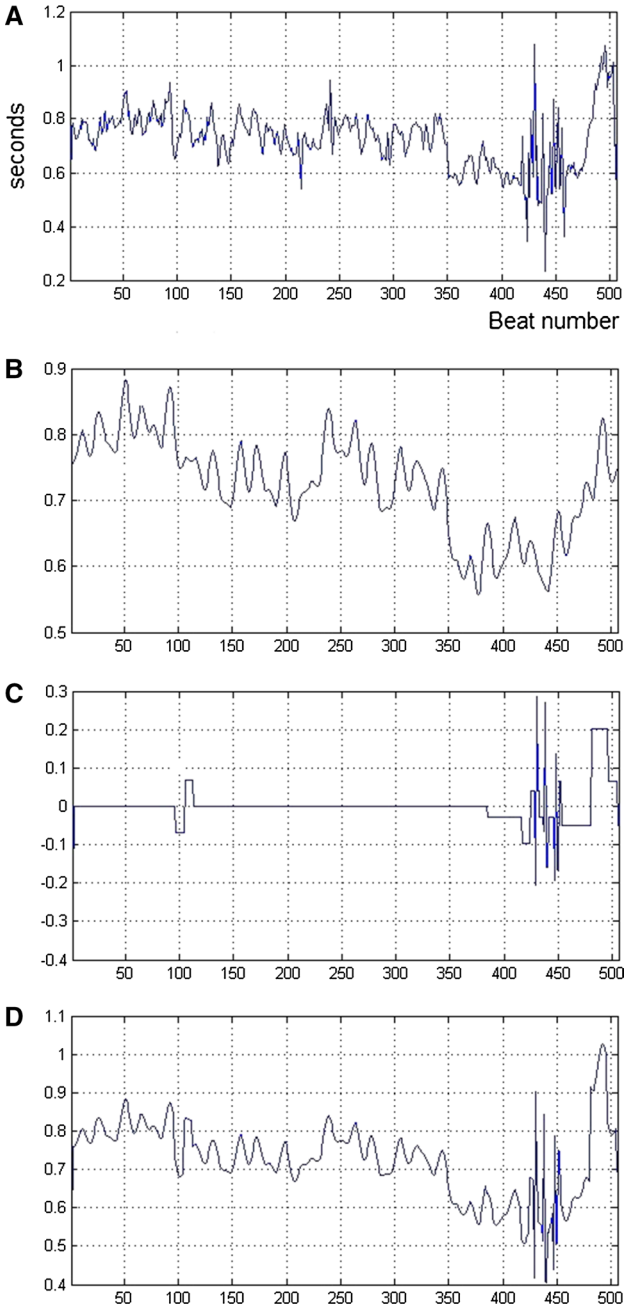

Fig. 3 Represents the OMP analysis of a different subject. Panel **a** represents the original signal. Panel **b** represents the OMP RR signal partial reconstruction, Fourier components only. Panel **c** represents the OMP RR signal partial reconstruction, wavelet components only. Panel **d** represents the combined reconstruction using all components both Wavelet and Fourier

to the baseline and no statistically significant changes regarding the pain decline period compared to the stable maximal pain period or the baseline. The WT showed a significant increase in the coefficients' density during the entire cold pressor test compared to the baseline period ($p < 0.05$). The baseline density was 0.043 ± 0.054 Hz, and the cold pressor test was 0.059 ± 0.052 Hz.

Analysis of the tachograms by the OMP algorithm showed that there was a significant increase in the wavelet coefficients' density during the pain incline period compared to the baseline ($p < 0.01$). The baseline density was 0.0056 ± 0.0036 Hz, and the pain incline period density was 0.055 ± 0.068 Hz. The density of the wavelet coefficients dropped during the stable persistent maximal pain period (though not statistically significant) and significantly increased again during the pain decline period to 0.024 ± 0.017 Hz ($p < 0.05$) this as compared to the stable maximal pain period and the baseline, marking out the periods of acute physiological changes (pain incline and pain decline periods). Comparison of the OMP calculated wavelet coefficient density during the entire cold pressor test to the baseline using a paired t test showed that there was a significant increase in the coefficients' density from 0.0056 ± 0.0036 Hz to 0.031 ± 0.039 Hz ($p < 0.001$).

Statistical analysis by the two-way ANOVA with repeated measures showed significant interaction between the methods (WT, OMP) and the physiological states (baseline and pain incline periods) ($F_{1,10} = 5.92$, $p = 0.035$), indicating that the proportional increase in wavelet coefficients during that period was significantly higher using the OMP algorithm as compared to the WT analysis. When the same analysis was applied to the entire protocol, as compared to the baseline period, this again yielded a significant interaction $F_{1,10} = 9.881$, $p < 0.01$, indicating that the proportional increase in wavelet coefficients during the entire cold pressor test was significantly higher using the OMP algorithm.

Analysis of the coefficients' amplitudes calculated by the two methods showed that the standard WT coefficients' amplitudes analysis by a log scale had a significant increase during the entire cold pressor test compared to the baseline ($F_{3,290} = 6.413$, $p < 0.001$), with some preference to the incline period [$t_{290} = 3.908$, $p = 0.001$(incline); $t_{290} = 2.6$, $p = 0.039$ (stable pain); $t_{290} = 2.85$, $p = 0.023$ (decline)]. The net effect was 17 % increase compared to the baseline.

The OMP algorithm wavelet coefficients' amplitude difference analysis had a suggestive increase in the amplitude between the baseline and the protocol period, and the overall effect was marginally significant ($F_{3,106} = 2.368$, $p = 0.075$); this was probably subject to the small number of wavelet coefficients sampled during the baseline. When looking at the different periods, the only suggestive significant difference was found between the baseline and incline period ($t_{106} = 2.544$, $p = 0.0732$).

The different figures show the range of signals and findings between the different subjects and the two methods. Figure 2b represents the signal's reconstruction of the RR signal by 40 standard WT coefficients. It

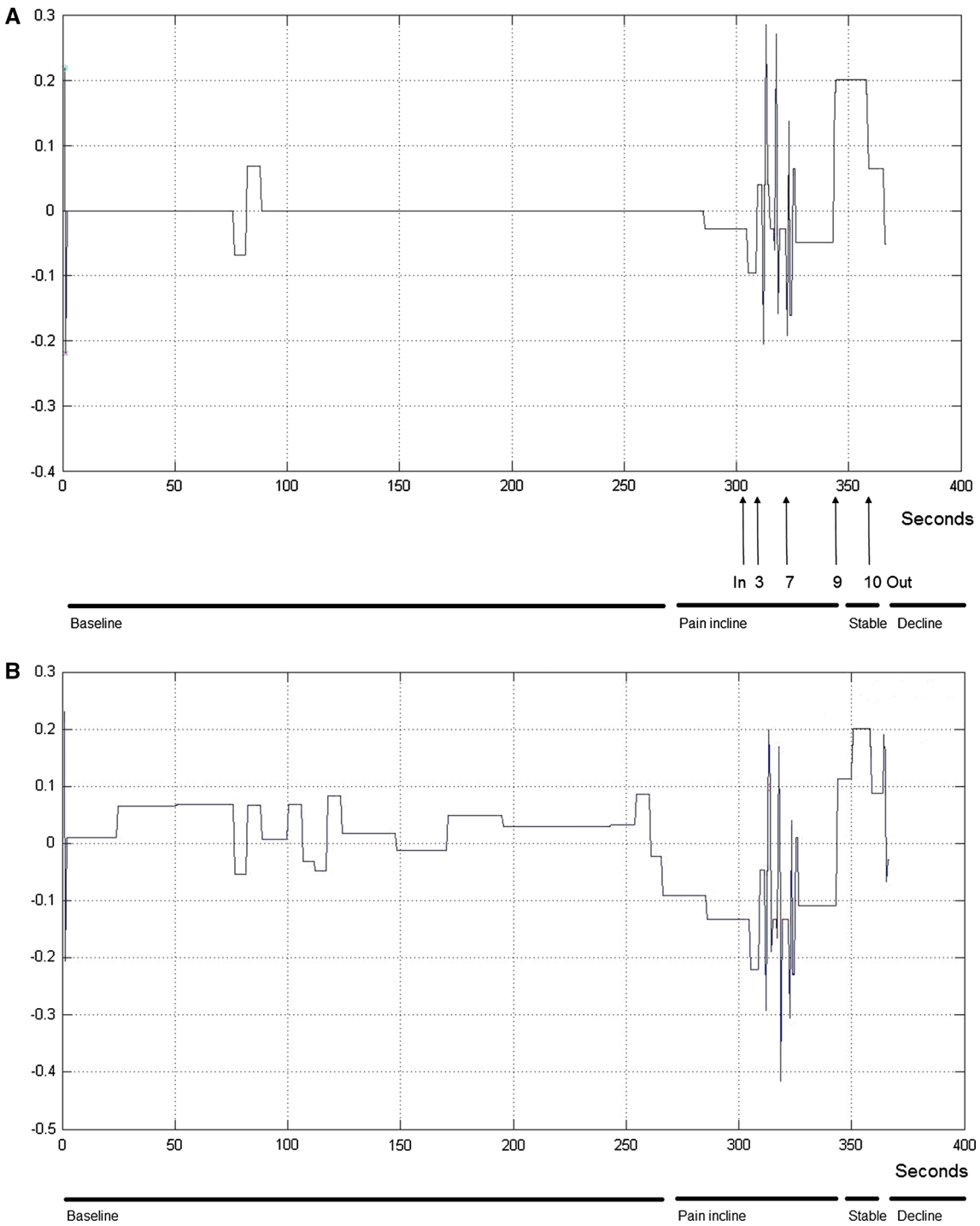

Fig. 4 Panel **a** represents the second subject's RR signal reconstruction from the wavelet coefficients only obtained by the OMP algorithm in Fig. 3c. The *x-axis* is translated to seconds, and the partial reconstruction is compared to the second subject's protocol indicated on the *x-axis*. Panel **b** represents the second subject's RR signal reconstruction from the wavelet coefficients obtained by **a** the standard wavelet transform. The *x-axis* as in panel **a** is translated to seconds. Note that unlike the previous sample, in this case both methods provide adequate detection of pain

is clear that pain detection in this reconstruction is not clear, while Fig. 2a represents the reconstruction of the same subject's signal using the OMP wavelet coefficients only. This method manages to simplify pain detection by quieting the baseline using the Fourier coefficients and emphasize the painful event by a set of high-density and

Table 1 Wavelet coefficient density using the two analysis methods are reported with the following notation #coefficients/#seconds (number of coefficients per seconds)

Subject	Standard wavelet transform coefficients' density (coefficients per seconds)					OMP wavelet coefficients' density (coefficients per seconds)				
	Baseline	Incline	Stable	Decline	Σ CPT	Baseline	Incline	Stable	Decline	Σ CPT
1	10/398 (0.025)	11/91 (0.12)	2/31 (0.064)	10/159 (0.0629)	23/281 (0.0818)	1/398 (0.0025)	5/91 (0.055)		5/159 (0.0314)	10/281 (0.0355)
2	12/414 (0.0289)	5/105 (0.0476)	1/100 (0.01)	13/335 (0.0388)	19/540 (0.0351)	1/414 (0.0024)	3/105 (0.028)		3/335 (0.0089)	6/540 (0.0111)
3	12/60 (0.2)	22/108 (0.203)			22/108 (0.203)	2/260 (0.0077)	16/108 (0.148)			16/108 (0.148)
4	3/482 (0.0062)	4/198 (0.0202)	6/113 (0.053)	4/240 (0.0156)	14/551 (0.0254)	2/482 (0.0041)	1/198 (0.005)	3/113 (0.0265)	3/240 (0.0125)	7/551 (0.0127)
5	7/328 (0.0213)	5/93 (0.0537)	2/98 (0.0204)	7/205 (0.0341)	14/396 (0.0353)	4/328 (0.0121)	2/93 (0.0215)		8/205 (0.039)	10/396 (0.0252)
6	13/346 (0.0375)	10/139 (0.072)			10/139 (0.072)	1/346 (0.0029)	3/139 (0.0216)			3/139 (0.0216)
7	4/397 (0.01)	3/98 (0.03)	23/287 (0.08)		26/385 (0.0675)	2/397 (0.005)	1/98 (0.0102)	6/287 (0.0209)		7/385 (0.0182)
8	2/425 (0.0047)	3/191 (0.015)	6/412 (0.0145)		9/603 (0.015)	1/425 (0.0024)	3/191 (0.0157)	5/412 (0.0121)		8/603 (0.0132)
9	12/258 (0.0465)	6/142 (0.0422)	4/135 (0.0296)	11/308 (0.035)	21/585 (0.0358)	1/258 (0.0039)	3/142 (0.211)	1/135 (0.0074)	2/308 (0.0065)	6/585 (0.0102)
10	17/328 (0.0518)	4/115 (0.0347)	9/360 (0.025)	10/120 (0.083)	23/783 (0.0293)	4/328 (0.0121)		4/360 (0.011)	6/120 (0.05)	10/783 (0.0128)
11	13/291 (0.0446)	5/89 (0.0561)			5/89 (0.0561)	2/291 (0.0069)	3/89 (0.0337)			3/89 (0.0337)

The periods are defined by the VASs. The incline period is from VAS 0–9, the stable period is during the cold pressor test (CPT) at maximal pain VAS 9 and 10, and the decline period is registered when the hand is taken out of the water

high-amplitude wavelet coefficients, thus pointing out the acute event. The partial reconstruction of the RR signal is correlated with the pain described by the subject, numbered by the VAS pain score. Unlike the first subject, the second subject's tachogram analysis portrayed in Figs. 3 and 4 has clear increase in wavelet coefficients' density and amplitude during the acute painful event, no matter what method was used (Fig. 4a, b) demonstrating the versatility and different findings we found in different subjects.

4 Discussion

Assessments of the autonomic heart rate changes during acute pain were evaluated in multiple studies, though no tool for objective pain detection has been successfully developed yet. Biological signals such as the ECG are non-stationary and non-uniform incorporating both static background frequencies and dynamic acute changes. The Fourier transform is ideal for analyzing signals consisting of pure harmonics, and the Wavelet transform is ideal for analyzing piece-wise smooth functions with discrete singular points. The OMP method allows the biological signal to be evaluated by both transforms, reconstructing the signal by an over-complete dictionary and decomposing it into its main components.

This study focused on heart rate analysis for acute pain detection using the WT and the OMP algorithm integrating the Wavelet and the Fourier transforms. In both methods, we examined the time-related wavelet coefficients looking to see whether any real-time detection of a painful stimulus can be made. When looking at the two methods separately, the standard WT analysis showed a significant increase in wavelet coefficients' density during the initial pain incline period and during the entire cold pressor test, as compared to the baseline period. Moreover, a significant rise in the wavelet coefficients' amplitudes was also observed. These findings show that heart rate analysis by the WT can acutely detect a painful event in real time without an obligatory delay anticipated using spectral analysis methods. Though wavelet coefficients do appear during baseline, the coefficients are significantly more prominent and more frequent as soon as pain commences.

Separate analysis by the OMP algorithm also showed a significant rise in the wavelet coefficients' density during the pain incline period, as well as during the pain decline period, depicting the acute autonomic changes. Similar to the WT analysis, the OMP analysis showed an overall significant increase in the wavelet coefficients' density during the entire cold pressor test compared to the baseline. An increase in the OMP wavelet coefficients' amplitudes during the painful event was only suggestive.

When comparing the two methods, a striking finding correlated with our hypothesis regarding heart rate analysis using the OMP algorithm. We found that during the baseline period there was an absolute reduction in wavelet coefficients number using the OMP analysis as compared to the WT analysis. This was attributed to the fact that during the baseline period there were minimal acute events, and thus, the wavelet coefficients charted by the WT during that period were represented now by OMP's Fourier transform coefficients, as functional harmonics. Thus, by using an over-complete Fourier/Wavelet dictionary, there were minimal wavelet coefficients during a physiological "quiet" period. Once the cold pressor test started, a growing density of large wavelet coefficients appeared representing the acute event.

Further comparison of the two methods by the two-way ANOVA with repeated measures showed a significant proportional increase in wavelet coefficients' density during the incline period in the OMP algorithm as compared to the WT analysis. When the same analysis was applied to the data of the entire protocol versus the baseline, this again yielded a significant proportional increase in wavelet coefficients. These findings demonstrate that the advantage of the OMP analysis has over the standard WT in analyzing a biological signal and decomposing it to its basic components, the functional harmonics and the acute events, thus enabling better detection of acute pain.

This study is an initial attempt to create an operator independent monitoring tool for acute pain detection using time-related algorithms. In the future, real-time signal analysis could be of clinical use due to its objective ability to mark out the exact initiation of pain. The ability of this system to point out objectively an acute painful event allows it to be used in clinical settings such as in patients under sedation or general anesthesia or in patients who are non-responsive but still endure pain. We should emphasize though that by using the tachogram this system analyzed only the heart rate. Any other information present in the ECG signal like AV conductance, QRS morphology and amplitudes, or ST segment changes was eliminated, and other potential information of signals currently available in the OR or in the ICU was also not considered. Moreover, the heart rate signal is non-specific and may reacts to many different stimuli and stress triggers. Acute events which cause rapid changes in heart rate like anxiety or seizures could affect the analysis and acute events could be charted, events that might not be discriminated from pain, though can be distinguished by the caregiver. On the other hand, medications which prevent tachycardia such as beta blockers might prevent appropriate heart rate response and blunt pain detection.

There are several limitations to this study which need to be pointed out. The studied subject group was relatively small and included both males and females. A study by Vallerand et al. [28] showed that there were gender differences regarding pain perception and thresholds. Moreover, this group of subjects included healthy adults with no cardiac or neurological background and without any history of chronic pain. It is still not clear how the heart rate reacts to pain in these patients and what adjustments will be needed in this system. Also, this experiment was that of a brief exposure to a painful stressor in a safe environment, and not that of the real world, where pain is oftentimes associated with mental distress, a factor which might alter or extenuated the results. It also should be noted that mental stress itself could alter the findings. The results here were not compared to mental stressors to evaluate the difference between pure mental stressors and the combined mental and painful stressors studied here.

Finally, this objective pain detection algorithm might be effective in unconscious and anesthetized patients. Studies are performed these days to evaluate whether sedation and analgesia drugs used daily in the operating room could alter the pattern of acute pain recognition.

5 Conclusion

Heart rate analysis by both the WT and the OMP algorithm has managed to point out significantly the painful event as it initiated without delay. This is the first study in which the OMP analysis method was used for acute detection of painful stimuli and proved it to be significantly sensitive, bringing us one step further in the quest of an objective acute pain detector.

To assess the method's accuracy, studies should be performed to correlate the OMP algorithm analysis with more signal processing methods and with objective markers for pain such as blood levels of serotonin or substance *P*. Moreover, this analysis was done off-line, allowing us to evaluate it as a whole. Further research should take place to implement the OMP algorithm as a continuous online system and evaluate its ability to generate real-time findings, correlating it to immediate events.

Compliance with ethical standards

Conflict of interest We declare that we have no conflict of interest.

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