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Wavelet Transform Cardiorespiratory Coherence Detects Patient Movement During General Anesthesia

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Abstract— **Heart rate variability (HRV) may provide anesthesiologists with a noninvasive tool for monitoring nociception during general anesthesia. A novel wavelet transform cardiorespiratory coherence (WTCRC) algorithm has been developed to calculate estimates of the linear coupling between heart rate and respiration. WTCRC values range from 1 (high coherence, no nociception) to 0 (low coherence, strong nociception). We have assessed the algorithm's ability to detect movement events (indicative of patient response to nociception) in 39 pediatric patients receiving general anesthesia. Sixty movement events were recorded during the 39 surgical procedures. Minimum and average WTCRC were calculated in a 30 second window surrounding each movement event. We used a 95% significance level as the threshold for detecting nociception during patient movement. The 95% significance level was calculated relative to a red noise background, using Monte Carlo simulations. It was calculated to be 0.7. Values below this threshold were treated as successful detection. The algorithm was found to detect movement with sensitivity ranging from 95% (minimum WTCRC) to 65% (average WTCRC). The WTCRC algorithm thus shows promise for noninvasively monitoring nociception during general anesthesia, using only heart rate and respiration.**

I. INTRODUCTION

Anesthesiology is commonly regarded as the practice of autonomic medicine. Noxious stimuli during surgery cause the autonomic nervous system (ANS) to invoke a stress response, increasing sympathetic tone and decreasing parasympathetic tone [1]. An excessive and prolonged sympathetic response increases the risk of suffering from peri-operative complications and delayed recovery. Indeed, the surgical stress response is a key factor in postoperative morbidity [2]. Anesthesiologists must therefore control the ANS by administering analgesic drugs.

There is currently no clinically proven and routinely used monitor of the ANS. Anesthesiologists are guided by observation and interpretation of trends in patients' vital signs, which are only indirect measures of nociception. Confounding factors such as pre-existing medical conditions and inter-patient variability cause difficulties in such indirect estimations. An automated nociception monitor that directly assesses ANS activity would be very useful for general anesthesia, providing anesthesiologists with feedback about the adequacy of analgesia. Heart rate variability (HRV) shows promise as a noninvasive nociception monitor [3], [4].

We have previously developed a wavelet transform cardiorespiratory coherence (WTCRC) algorithm to measure autonomic balance [5]. WTCRC estimates the strength of linear coupling between the heart rate (HR) and respiration in the joint time/frequency domain. The algorithm provides a measure of respiratory sinus arrhythmia (RSA), which has been shown to reflect the balance between the sympathetic and parasympathetic tones [6]. WTCRC tracks respiration (and thus RSA) as it moves in the time/frequency plane, by using the known respiratory frequency calculated from a respiratory wave. In so doing, the algorithm entirely eliminates the traditional concept of frequency bands, allowing it to function in a wider range of conditions than other time/frequency methods. We have previously shown that WTCRC correlates with the LF/HF power ratio, and that it can function in a wider range of conditions, such as when the respiratory frequency is less than 0.15 Hz [5].

We wish to assess the performance of WTCRC in measuring nociception, but there is no gold standard for comparison. Anesthetized patients clearly cannot report their level of pain, and no other algorithm has been proven as an accurate measure of nociception. Changing levels of surgical stimuli and anesthetic drugs lead to variable levels of nociception during surgery, and the precise level at any given point in time is unknown. Nevertheless, it may be possible to assess WTCRC's sensitivity to nociception.

Patient movement is a symptom of inadequate analgesia [7], and is a strong sign that the patient is responding to nociceptive stimuli. The WTCRC algorithm should reflect a loss of coherence during movement events, if it is truly sensitive to nociception.

This paper describes the WTCRC algorithm and investigates its sensitivity to movement events in patients receiving general anesthesia during surgery.

II. METHOD

A. Wavelet Transform Cardiorespiratory Coherence

The WTCRC algorithm first calculates the continuous wavelet transform for the heart rate time series (tachogram) and a respiration wave. At any given scale, the wavelet transform is given by:

$$W_n(s) = \sum_{n'=0}^{N-1} x_{n'} \Psi^* \left[\frac{(n'-n)\delta t}{s} \right], \qquad (1)$$

where x_n is the input time series, n is the time index, s is the scale, δt is the sampling time, and the asterisk

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(*) is the complex conjugate operator. We use a complex Morlet mother wavelet, as its scales are directly related to Fourier frequencies. The result is a 2D matrix of wavelet coefficients at different times and scales. We denote the wavelet coefficients for the tachogram and respiration as W_n^T and W_n^R, respectively.

From the wavelet coefficients, the algorithm calculates the wavelet power spectrum for each signal, as well as the cross power spectrum:

$$\begin{aligned} W_n^{TT}(s) &= W_n^T(s) W_n^{T*}(s), \\ W_n^{RR}(s) &= W_n^R(s) W_n^{R*}(s), \\ W_n^{TR}(s) &= W_n^T(s) W_n^{R*}(s). \end{aligned} \tag{2}$$

Power densities are then smoothed in time with a Gaussian window ($e^{-t^2/2s^2}$) and in scale with a rectangular window (length 0.6 x scale).

The algorithm then calculates the coherence estimator, as the squared absolute value of the smoothed cross-wavelet spectrum normalized by the smoothed absolute values of the individual wavelet spectra:

$$\hat{C}_n^2(s) = \frac{\left|\left\langle W_n^{TR}(s) \cdot s^{-1} \right\rangle\right|^2}{\left\langle \left|W_n^{TT}(s)\right| \cdot s^{-1} \right\rangle \left\langle \left|W_n^{RR}(s)\right| \cdot s^{-1} \right\rangle}, \tag{3}$$

where the angled brackets ($\langle\rangle$) denote the smoothing operator. The coherence estimator is a 2D matrix of coherence values at each time and frequency.

Finally, the algorithm extracts the coherence values at the known respiratory frequency (RSA) at each point in time, using respiratory rate (RR) values calculated from the respiration wave *a priori*. WTCRC outputs a 1D vector of time-varying coherence values from the respiratory frequency. Coherence can range from 0 (no coherence) to 1 (perfect coherence).

B. Movement Detection Threshold

We use the 95% significance level as the threshold for detecting nociception during patient movement. The significance level reflects the results of a hypothesis test. The statistical significance of the wavelet spectral power is estimated relative to the null hypothesis that it is generated by a random background noise process. The result is the minimum coherence value required for rejecting the null hypothesis with 95% confidence. If the wavelet power is significantly stronger than the background noise, then it is assumed to be true coherence (no nociception). Otherwise, we cannot reject the null hypothesis that it is not true coherence (nociception). Thus, the 95% significance level serves as our threshold for detecting patient movement.

We model the background as red noise using a lag-1 autoregressive process. Red noise power increases with decreasing frequency, and is a reasonable model for the HRV (e.g. DC and VLF power is much higher than LF and HF power). The red noise Fourier spectrum is given by [8]:

$$P_k = \frac{1 - \alpha^2}{\left|1 - \alpha e^{-2i\pi k}\right|^2}, \tag{4}$$

where α is the lag-1 autocorrelation and k defines the frequency index. This process is chi-square distributed with two degrees of freedom (χ_2^2) because we are using the complex Morlet wavelet. The probability that the wavelet power is greater than the background noise is given by:

$$D\left(\frac{\left|W_n^X(s)\right|^2}{\sigma_X^2} < p\right) = \frac{P_k \chi_2^2(p)}{2} \tag{5}$$

The hypothesis test is performed with a Monte Carlo simulation of 10,000 randomly generated red noise time series.

C. Clinical Protocol & Data Collection

Following ethics approval and informed consent, data were collected from 39 healthy pediatric patients receiving general anesthesia during dental surgery. Subjects were aged 3-6 years, had ASA physical status I or II, were free of cardiorespiratory disease, and were not taking medications that alter ANS function. Subjects were anesthetized with propofol and remifentanil. Surgeries provided multiple periods of nociceptive stimuli, including dental dam insertions, tooth extractions, cavity drillings, and cap insertions.

Physiological data were recorded throughout each case. The electrocardiogram (ECG) and capnometry (CO_2) waves, as well as the RR trend, were recorded using Datex/Ohmeda S/5 Collect software (GE Healthcare, Helsinki, Finland). The ECG was recorded at 300 Hz, CO_2 at 25 Hz, and RR (from capnometry) at 0.1 Hz. A research assistant annotated the data in real-time with markers identifying patient movement events.

D. Data Analysis

Data were first manually inspected and selected for analysis. Case annotations were searched to find all recorded patient movement events. Movement events were only retained for analysis if they occurred during the stable phase of anesthesia, when the patient was mechanically ventilated, and when the respiration and ECG waves were free of significant artifacts. The following were considered to be movement events:

- moving limbs or torso,
- tensing muscles,
- biting/clenching teeth,
- coughing,
- surgeon reporting a patient response to stimulation.

In total, 60 movement events were retained for analysis.

Heart rate and respiration signals were prepared for analysis. Data segments were first extracted around each patient movement event. Each segment was at least 2 minutes long to ensure the analysis was not corrupted by edge artifacts. ECG R peaks were detected using a filter bank algorithm [9]. Each R-R interval series was converted into a tachogram, and then resampled onto an evenly-spaced 4 Hz grid using Berger's algorithm [10]. The flow wave was downsampled to 4 Hz using standard low pass filtering and decimation. The RR trend (derived from the flow wave) was upsampled to 4 Hz using a repeater. Minor tachogram artifacts were manually detected and corrected.

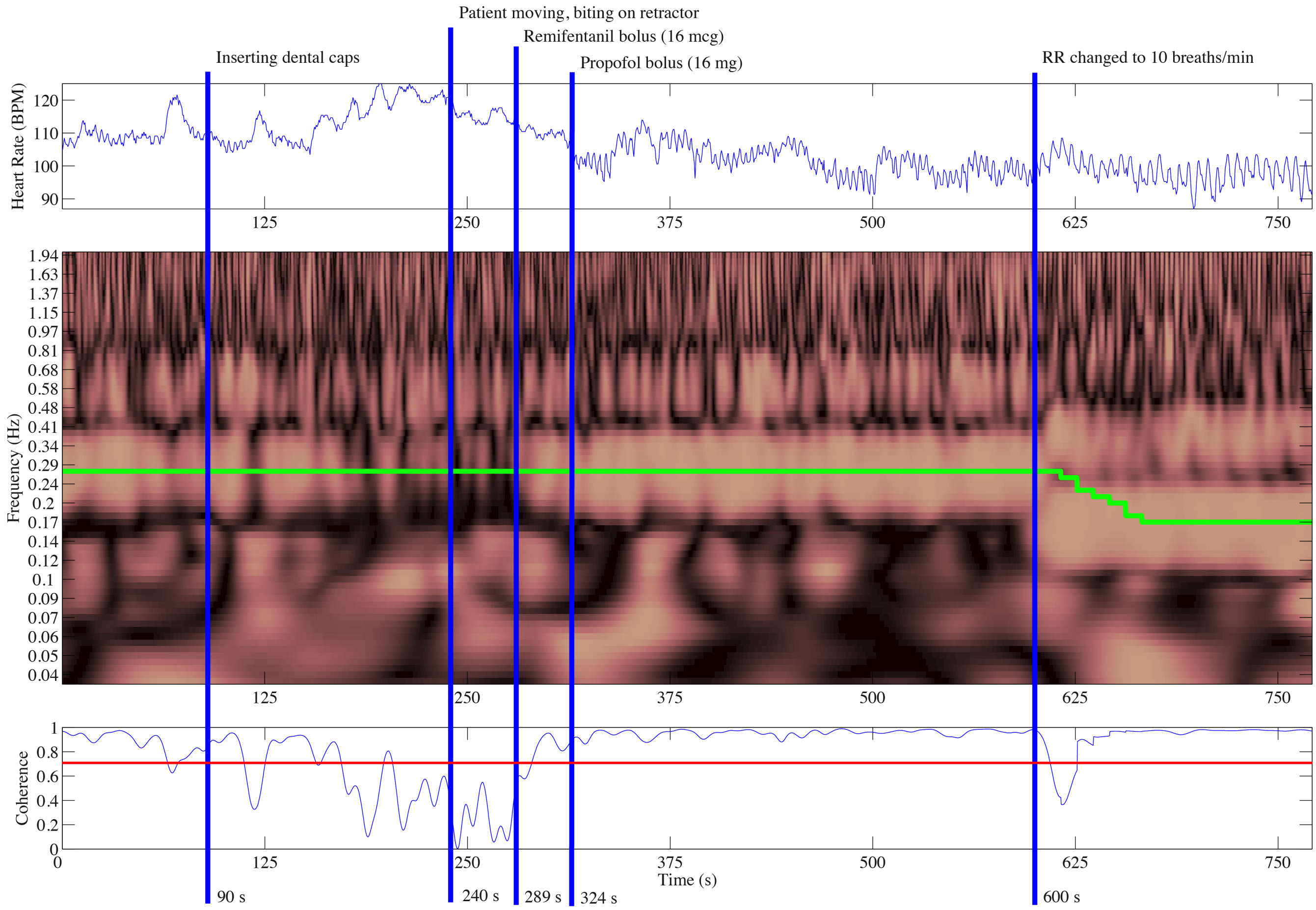

Fig. 1. Example WTCRC analysis. Top plot: tachogram. Middle plot: coherence map. Bright areas indicate high coherence. Horizontal green line indicates the respiratory frequency. Bottom plot: coherence at the respiratory frequency. Horizontal red line indicates the 95% significance level. Vertical blue lines denote clinical events. A patient movement event (biting on retractor) was recorded at time t = 240 s. Coherence is below the 95% significance level threshold near the movement event, but recovers to a statistically significant value after the patient receives additional anesthetic drugs (propofol and remifentanil boluses).

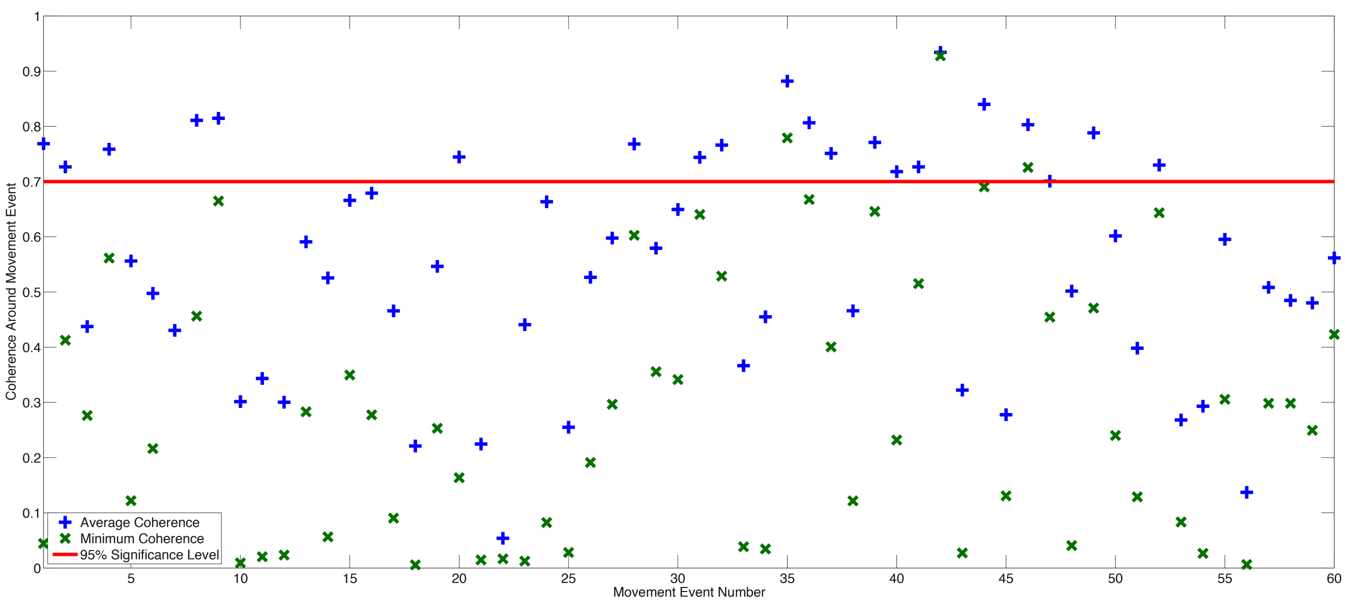

Fig. 2. Nociception detection results for each movement event. Coherence below the 95% significance level (red line) is a successful detection.

WTCRC was calculated over each data segment, and a 30 second window surrounding each movement event was extracted (15 seconds on each side of the event). The effects of movement should be manifested within the window. Two different metrics were calculated for each window: average and minimum WTCRC.

III. RESULTS

The outcome of the Monte Carlo simulation suggests that the 95% significance level is approximately 0.7. We thus used this value as the movement detection threshold.

Fig. 1 illustrates an example WTCRC analysis of a single patient movement event. Fig. 2 presents the analysis results across all patient movement events.

The minimum and average coherence values were below the threshold (i.e. movement detected) during 57/60 (95%) and 39/60 (65%) patient movement events, respectively.

IV. DISCUSSION & CONCLUSION

We have developed a novel WTCRC algorithm for monitoring nociception during general anesthesia. The algorithm estimates the strength of linear coupling between the heart rate and respiration. It measures autonomic state based solely on RSA, which has been shown to reflect the net balance between sympathetic and parasympathetic tones [6]. WTCRC enhances previous work by analyzing the coherence only at the known respiratory frequency. In so doing, it eliminates the concept of HRV frequency bands. The algorithm performs well even when the respiratory frequency is outside the HF band [5].

We have shown that WTCRC can detect patient movement with high sensitivity in patients receiving general anesthesia. We estimated a 95% significance level of 0.7 for WTCRC using Monte Carlo simulations, to serve as a movement detection threshold. Using this threshold, we achieved a sensitivity of 95% for minimum coherence, and 65% for average coherence.

These results suggest a possible avenue for future algorithm tuning. Choice of metric (e.g. minimum or average coherence) and window length (e.g. 30 seconds) could be adjusted to tune the WTCRC results. By using shorter windows or minimum coherence, we can make the algorithm very sensitive to nociception. Conversely, we can decrease the sensitivity by averaging over longer windows. Anesthesiologists could adjust the tuning during surgery to reflect their concern for the patient. Patients at greater risk may warrant a higher sensitivity than others. Adjusting an algorithm's sensitivity typically results in a tradeoff with specificity.

Assessing WTCRC's specificity is very difficult, however, and is beyond the scope of this work. While patient movement events are strong indicators of true positive responses to nociception, there is no corresponding indicator of true negative responses. Lack of movement does not mean lack of response. A high level of nociception is required to cause patient movement. Subcritical levels of nociception still affect the patient, but do not cause movement. As such, we cannot use periods without movement as true negatives for nociception.

Future work will involve adapting the WTCRC algorithm to run in real time, which is essential for real-world clinical use. Real-time adaptation is nontrivial; in particular, we must address the problems of edge artifacts and runtime complexity. We will also investigate methods of applying WTCRC during periods of spontaneous ventilation. Spontaneous ventilation can be highly nonstationary, and tends to produce noisy coherence estimates. This is especially problematic in anesthetized patients, who may be semi-apneatic. Methods could conceivably be developed to deal with these conditions.

WTCRC can be used to detect patient movement with high sensitivity. The algorithm shows promise as a monitor of nociception during general anesthesia. In the future, it could provide anesthesiologists with feedback about the adequacy of analgesia in real time, increasing patient safety during surgery.

V. ACKNOWLEDGMENTS

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