# Wavelet Transform Cardiorespiratory Coherence for Monitoring Nociception

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## Abstract

*Heart rate variability (HRV) may provide anesthesiologists with a noninvasive tool for nociception monitoring during general anesthesia. A novel wavelet transform cardiorespiratory coherence (WTCRC) algorithm was used to calculate estimates of the linear coupling between heart rate and respiration. WTCRC was tested on clinical data from 19 pediatric patients receiving general anesthesia during dental surgery. WTCRC decreased during nociception, and increased following additional anesthetic drugs. Data were divided into categories with normal respiratory rate (RR) (in the HF band) and low RR (in the LF band), then split into 2-minute windows. WTCRC and LF/HF were calculated for each window and compared in each category. The algorithms showed correlations of -0.5506 and -0.1403 for data with normal and low RR, respectively. WTCRC and LF/HF are comparable when the RR is normal, and WTCRC significantly outperforms when the RR is low.*

## 1. Introduction

Anesthesiology is commonly regarded as the practice of autonomic medicine [1]. Noxious stimuli during surgery cause the autonomic nervous system (ANS) to invoke a stress response, increasing sympathetic tone and decreasing parasympathetic tone. 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 post-operative morbidity [2]. Anesthesiologists must therefore control the ANS by administering analgesic drugs.

There is currently no clinically available 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].

The Fourier-based HRV LF/HF power ratio is the most widely used measure of autonomic balance, but is inadequate for nociception monitoring. This analysis transforms the HRV to the frequency domain, and divides the resulting power spectrum into low frequency (LF, 0.04-0.15 Hz) and high frequency (HF, 0.15-0.4 Hz) bands. LF/HF is the ratio of powers in these bands. Fourier analysis is poorly localized in time, requiring data windows of at least 2 minutes for accurate results. Furthermore, the LF/HF ratio theory itself is flawed. Most believe that the LF band power is affected solely by sympathetic tone, and that the HF band power is affected solely by parasympathetic tone [5]. Some studies have cast doubt on this simple view of the frequency bands. A study of HRV under sympathetic blockade suggests that respiratory sinus arrhythmia (RSA) in the HF band is driven by parasympathetic tone and restrained by sympathetic tone [6]. The observed HF band power thus reflects the net balance of the two ANS branches. Finally, rigid HF band limits at 0.15 and 0.4 Hz are not guaranteed to capture RSA. If the respiratory rate (RR) drops below 9 breaths/min, the RSA power will fall in the LF band, significantly distorting the LF/HF ratio. Some work has been done to adjust HF band limits dynamically, based on the heart rate (HR) and RR [7].

Recently, a novel wavelet transform coherence (WTC) algorithm was applied to HRV analysis [8]. The algorithm estimates the strength of linear coupling between the HR and respiration, averaged over the HF band. In a body position experiment, WTC was shown to decrease during posture change, and to stabilize at lower levels while standing upright as compared to laying supine. WTC may be a better measure of autonomic balance than LF/HF, but it still uses rigid HF band limits.

We have developed an enhanced WTC algorithm, dubbed wavelet transform cardiorespiratory coherence (WTCRC), that eliminates the concept of frequency bands. Most HRV studies use conscious, spontaneously ventilated subjects, leading to a highly variable RR. In contrast, patients receiving general anesthesia are unconscious and usually mechanically ventilated, and thus have a precise and locally stationary RR. WTCRC estimates coherence specifically at the respiratory frequency.

This paper describes the WTCRC algorithm and investigates its performance on clinical data in comparison with the LF/HF ratio.

## 2. Method

### 2.1. Wavelet transform cardiorespiratory coherence

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

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

where $x_n$ is the input time series, $n$ is the time index, $s$ is the scale, $\delta t$ is the sampling time, and the asterisk ($^*$) is the complex conjugate operator. 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:

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

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 at each point in time, using 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).

### 2.2. Clinical protocol & data collection

Following ethics approval and informed consent, data were collected from 20 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. Nociceptive stimuli were often followed by an increase in the anesthetic infusion.

Ventilatory parameters were modified during each case, to investigate their effect on HRV. Each case began with a low RR of 8 breaths/min, and the RR was later increased to 16 breaths/min. Ventilatory changes were overridden if the $CO_2$ exceeded acceptable limits.

Physiological data were recorded throughout each case. The electrocardiogram (ECG), capnography ($CO_2$, $O_2$), and spirometry (flow, pressure) waves, as well as RR trends, were recorded using Datex/Ohmeda S/5 Collect software (GE Healthcare, Helsinki, Finland). Waves were recorded at 300 Hz, and trends at 0.1 Hz. Data were annotated with markers describing relevant surgical events (e.g. nociceptive surgical stimuli, patient movement, changes in anesthetic administration, ventilatory changes).

### 2.3. Data analysis

Data were first manually selected and categorized for analysis. Each case was visually inspected, and segments with significant ECG or respiratory artifacts were excluded from analysis. One case was affected by significant ECG artifacts throughout, and was thus excluded. The remaining 19 cases comprised a total of 730 minutes of clean data. Case data were divided into two categories: those with normal RR (in the HF band, $>=$ 9 breaths/min) and those with low RR (in the LF band, $<$ 9 breaths/min). Normal and low RR categories comprised a total of 498 and 232 minutes of data, respectively. Subsequent processing was entirely automated in Matlab (The Mathworks Inc., Natick, MA).

Heart rate and respiration signals were prepared for analysis. ECG R peaks were detected using a filter bank algorithm [9]. Each R-R interval series was converted into a tachogram. The tachogram was resampled onto an evenly-spaced 4 Hz grid using Berger's algorithm [10]. The respiratory flow wave was used for analysis in 18 cases. Spirometry was unavailable in one case, and the $CO_2$ wave was used instead. The respiratory wave was downsampled to 4 Hz using standard low pass filtering and decimation. The RR trend (derived from the $CO_2$ wave) was upsampled to 4 Hz using a repeater. Minor tachogram artifacts were

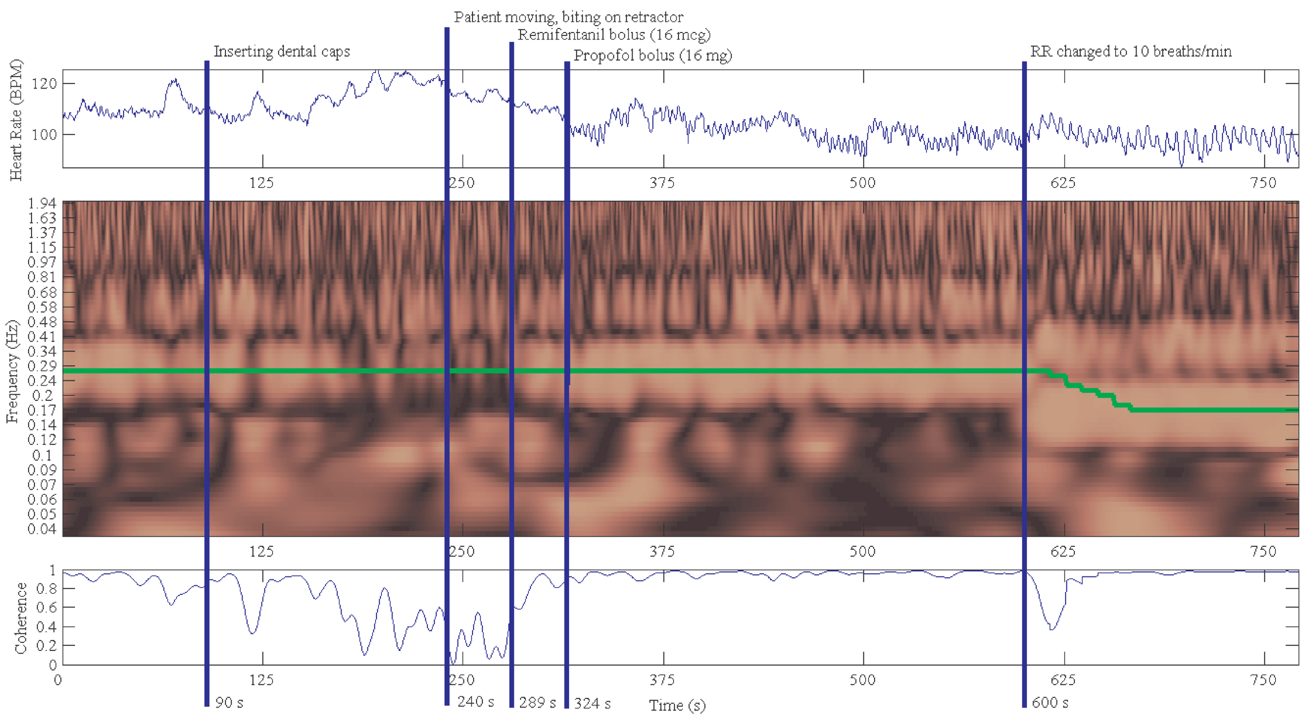


Figure 1. Example WTCRC analysis. Top plot: tachogram. Middle plot: coherence map. Bright areas indicate high coherence. Horizontal green line indicates the respiratory frequency. Bottom plot: coherence at the respiratory frequency. Vertical blue lines denote clinical events.

detected with a single level stationary wavelet transform decomposition, and corrected with a localized median filter. Data were divided into 2 minute windows for analysis.

The LF/HF ratio was calculated for each window. A Hamming window was first applied to the tachogram, to suppress edge artifacts. The tachogram's power spectrum was then computed with a Fourier transform. The resulting power spectrum was used to calculate the normalized LF/HF ratio.

WTCRC was calculated for each window. Standard data windowing is ineffective at eliminating wavelet edge artifacts; instead, the tachogram, respiration, and RR waves were padded at each end with 30 seconds of data from the preceding and succeeding windows. WTCRC was calculated on the padded data, with a complex Morlet mother wavelet analyzing to 96 scales. The padding was then removed from the resulting WTCRC. Finally, WTCRC was averaged over each window to produce a single coherence estimate for direct comparison with LF/HF.

## 3. Results

WTCRC consistently decreased during periods of nociception, and increased following additional anesthetic drugs, regardless of the RR (Fig. 1). The LF/HF ratio was erratic when the RR was low, and did not respond to nociceptive and analgesic events.

Estimates of autonomic balance from WTCRC and LF/HF were compared for each window. Comparisons were separated into the normal and low RR categories. The categories comprised 249 and 116 windows, respectively. Linear regressions were used to determine the correlation between the two algorithms. When the RR was in the HF band (normal RR), the algorithms had a correlation of -0.5506. When the RR was in the LF band (low RR), correlation dropped to -0.1403.

## 4. 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 balance 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, we have eliminated the concept of HRV frequency bands. The algorithm performs well even when the respiratory frequency is outside the HF band.

Edge artifacts are a limitation of WTCRC analysis. The data must be padded to eliminate the artifacts, which pro-

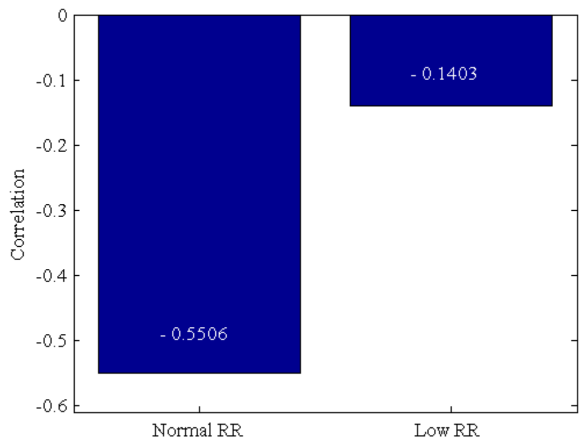


Figure 2. Correlation of average WTCRC vs. LF/HF ratio, for data with normal and low RRs.

duces a time lag in real-time analysis. Though we used 30 seconds of padding in our method, the padding could be much shorter in practice. Edge artifact width depends on the respiratory frequency; higher frequencies have shorter edge artifacts. The padding width could thus be dynamically adapted to the current RR. In the future, we will investigate alternative approaches to eliminating edge artifacts, with the goal of performing ultra short term ANS monitoring in real time.

WTCRC performed well compared to the LF/HF ratio in testing on clinical data. LF/HF is not a gold standard for comparison, but it is the most widely used measure of autonomic balance. Some correlation is therefore desirable, but perfect correlation would suggest that WTCRC is no better than LF/HF. WTCRC and LF/HF showed a moderate correlation when the RR was normal (in the HF band), and almost no correlation when the RR was low (in the LF band). When the RR was low, WTCRC continued to function properly while LF/HF did not. The LF/HF ratio performance could be improved by adopting respiratory frequency localization similar to WTCRC.

WTCRC is very highly localized in time. Accuracy of the LF/HF ratio begins to decrease when the analyzed window is shorter than 2 minutes. Conversely, WTCRC can detect changes in autonomic balance in less than one second. Our method of averaging WTCRC over each window was an artificial measure taken for comparison with LF/HF, and would not be performed in practice.

WTCRC consistently decreased during periods of nociception, and increased following additional anesthetic drugs, regardless of the RR (Fig. 1). It responded quickly to changing autonomic balance. WTCRC should be a better nociception monitor than the traditional LF/HF ratio.

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