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Spike detection in human muscle sympathetic nerve activity using the kurtosis of stationary wavelet transform coefficients

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Abstract

The accurate assessment of autonomic sympathetic function is important in the diagnosis and study of various autonomic and cardiovascular disorders. Sympathetic function in humans can be assessed by recording the muscle sympathetic nerve activity, which is characterized by synchronous neuronal discharges separated by periods of neural silence dominated by colored Gaussian noise. The raw nerve activity is generally rectified, integrated, and quantified using the integrated burst rate or area. We propose an alternative quantification involving spike detection using a two-stage stationary wavelet transform (SWT) de-noising method. The SWT coefficients are first separated into noise-related and burst-related coefficients on the basis of their local kurtosis. The noise-related coefficients are then used to establish a threshold to identify spikes within the bursts. This method demonstrated better detection performance than an unsupervised amplitude discriminator and similar wavelet-based methods when confronted with simulated data of varying burst rate and signal to noise ratio. Additional validation on data acquired during a graded head-up tilt protocol revealed a strong correlation between the mean spike rate and the mean integrate burst rate ($r = 0.85$) and burst area rate ($r = 0.91$). In conclusion, the kurtosis-based wavelet de-noising technique is a potentially useful method of studying sympathetic nerve activity in humans.

Keywords: Wavelet transform; Spike detection; Muscle sympathetic nerve activity; Higher order statistics; Humans

1. Introduction

Accurate assessment of autonomic function is important in the study and diagnosis of disorders such as essential hypertension (Wallin and Sundlof, 1979; Mark, 1996; Gudbjornsdottir et al., 1996), orthostatic intolerance (Furlan et al., 1998), and congestive heart failure (van de Borne et al., 1997). Autonomic sympathetic function can be assessed in humans by direct recordings of the muscle sympathetic nerve activity (MSNA) (Hagbarth and Vallbo, 1968).

The general appearance of the human MSNA has been described as heartbeat-synchronous discharges from a group of sympathetic neurons, separated by periods of neural silence (Wallin and Fagius, 1988) (e.g., see Fig. 2; Section 2.3). These bursts of activity are coupled to changes in the blood pressure and cardiac output through the baroreceptor reflex (Pagani et al., 1997; Furlan et al., 2000; Charkoudian et al., 2005). The most widely used MSNA processing method involves using an R–C circuit to rectifying and integrate the neurogram to achieve its envelope (Delius et al., 1972; Wallin and Sundlof, 1979), a signal known as the integrated-MSNA (Diedrich et al., 2003). At that point, bursts are identified and sympathetic activity can be quantified in terms of burst frequency (bursts/min), burst incidence (bursts/100 heart beats) or burst area rate (arbitrary units^2/min) (Sundlof and Wallin, 1977; Sugiyama et al., 1996).

Quantification of the MSNA using bursts in the integrated neurogram has its limitations. For instance, none of the burst parameters are capable of conveying whether a large burst is generated by a few large amplitude sympathetic spikes (or artifacts) or many small amplitude spikes firing in rapid succession. Also, the amount of pass band noise integrated into each burst is dependent on the signal-to-noise ratio (SNR) of each recording, making it difficult to compare the arbitrary unit burst amplitudes and areas across subjects.

An alternative solution to the integrated MSNA quantification problem is to implement a spike detection algorithm in the raw neurogram which allows for the possibility of subse-

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quent, automated sorting of spikes into classes derived from individual single unit neurons (Diedrich et al., 2003). Single-unit recordings have identified important differences in diseases such as congestive heart failure and hypertension which were not demonstrated in the multiunit burst rate (Macefield et al., 1999; Macefield and Wallin, 1999; Mary and Stoker, 2003). Since these single unit recordings are extremely difficult to achieve and sustain manually (Wallin, 2004), automated spike detection and classification methods will be useful in this area.

Automated wavelet-based methods have been successful in detecting and classifying neural spikes in typical colored Gaussian noise (Letelier and Weber, 2000; Nakatani et al., 2001; Oweiss and Anderson, 2002; Nenadic and Burdick, 2005). In particular, a wavelet-based spike detection method has been shown to outperform common, automated amplitude discriminators in the detection of human sympathetic spikes under varying signal to noise ratios (Diedrich et al., 2003). However, the parameters of this algorithm were optimized from recordings during a supine resting state, and its detection performance was not examined at higher or lower spike rates (Diedrich et al., 2003).

One major problem common to most spike detection techniques is the accurate estimation of noise level in the raw neurogram independent of the existing spike rate (Brychta et al., 2006). For example, in the raw MSNA neurogram, the shape of the amplitude distribution is nearly Gaussian during periods of neural silence (e.g., see Fig. 2; Section 2.3), but during a burst of neural activity, the presence of neural spikes changes the amplitude distribution significantly and most common noise estimators overestimate the noise level, leading to incorrect spike rate estimation.

To address this problem, we propose a novel two-stage wavelet-based spike detection approach that takes advantage of the bursting nature of the sympathetic nerve activity. This method uses the local kurtosis to classify wavelet coefficients as belonging to Gaussian pure-noise segments or non-Gaussian signal-plus-noise (burst) segments. The noise-related coefficients will then be used to establish a threshold which can subsequently be applied to the burst-related coefficients. The parameters of the two-stage wavelet method will be optimized using simulated MSNA burst data and validated against common integrate burst measures using recordings made during a head-up tilt protocol.

We plan to investigate the performance of the two-stage kurtosis spike detection method, several common wavelet-based spike detection schemes, and a more traditional amplitude discriminator using simulated sympathetic nerve signals with varying burst rate and SNR. We hypothesize that the two-stage kurtosis spike detection method will have a more robust performance than other commonly used spike detection schemes in terms of sensitivity and specificity across spike rate and noise levels.

2. Methods

2.1. Instrumentation and recording conditions

MSNA was recorded from the peroneal nerve (Vallbo et al., 1979). A unipolar tungsten electrode with an uninsulated tip, diameter 1–5 μm and shaft diameter 200 μm (Frederick Haer and Co., Bowdoinham, MA, USA), was inserted into the muscle nerve fascicles of the peroneal nerve at the fibular head for multi-unit recordings. Raw nerve activity was amplified with a total gain of 100,000, band pass filtered from 0.7 to 2 kHz (662C-3 Nerve Traffic Analysis System, University of Iowa, Iowa City, USA), and recorded. The filtered nerve signal was also placed through an *R–C* integrating circuit with a 0.1 s time constant and the output (integrated MSNA) was simultaneously recorded. Satisfactory recordings of muscle sympathetic nerve activity were defined by: (1) heart pulse synchronicity; (2) facilitation during Valsalva straining and suppression during the hypertensive overshoot after release; (3) increases in response to breath-holding; and (4) no change during tactile or auditory stimulation (Delius et al., 1972).

The continuous blood pressure (BP) waveform was measured by photoplethysmographic-based volume clamp method (Penaz, 1973) with a finger cuff on the middle finger of the non-dominant hand (Finapres, Ohmeda, Englewood, CO, USA). Respiration was measured using a pneumobelt (Pneumotrace II; UFI, Morro Bay, CA). All data were acquired at 5000 Hz, 14 bit resolution using the Windaq data acquisition system (DI-720, DATAQ Instruments, Akron, OH) and analyzed offline with custom software written in the PV Wave (Visual Numerics Inc., Houston, TX) and MATLAB (Mathworks; Natick, MA) environments.

2.2. Signal processing

2.2.1. Wavelet decomposition

The initial sympathetic spike detection technique proposed by Diedrich et al. (2003) used the discrete wavelet transform (DWT) to decompose the nerve signal into several frequency sub-bands of wavelet coefficients. However, the DWT lacks translation invariance, meaning that a completely different set of wavelet coefficients arises from DWT decomposition when the signal is shifted, or translated, in time (Liang and Parks, 1996). The absence of translation invariance can be detrimental in the de-noising (Silverman, 1999) and detection (Kim and Kim, 2003; Brychta et al., 2006) of transient neural spikes. Alternatively, the stationary wavelet transform (SWT) is translation invariant, and has been shown to improve sympathetic spike detection in mice (Brychta et al., 2006).

The SWT decomposition process (Mallat, 1991) is described by Eqs. (1) and (2). A signal, f, is projected onto a dyadically-spaced set of scales (spaced using a base of 2, i.e., scale $= 2^j$), or levels (level $j = \log_2(\text{scale } 2^j)$), using a set of *level dependent quadrature mirror decomposition filters*, h_j and g_j, that have respective band-pass and low-pass properties specific to each wavelet basis (Mallat, 1989). The broad scale, or *approximation*, coefficients, a_j, are convolved separately with g_j and h_j. This process splits the a_j frequency information roughly in half, partitioning it into a set of fine scale, or *detail* coefficients, d_{j+1}, and a coarser set of approximation coefficients, a_{j+1}. During the next level of processing, a zero is placed in between each consecutive value found in the g_j and h_j filters (i.e., up-sampling by two) to achieve the g_{j+1} and h_{j+1} filters. This procedure can be iteratively continued until the desired level of decomposition,