Analysis of the Relationship between Muscle Sympathetic Nerve Activity and Blood Pressure in Humans using Linear and Nonlinear Modelization

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Abstract: We modelize the relationship between muscle sympathetic nerve activity (MSNA) and mean blood pressure (MBP) under baseline conditions in humans. Linear and nonlinear approaches were used. In the low frequency band, the linear approximation was found to be quite accurate. The relationship between these signals was mainly unidirectional: MBP regulates MSNA. In the full frequency band, it has been shown that the nonlinear model was better than the linear one. Model validation was performed with MSNA time waveform reconstruction from MBP; nonlinear techniques proved to be more adequate.

INTRODUCTION

In humans, several studies have examined the relationship between different cardiovascular signals such as the arterial blood pressure (BP), instantaneous lung volume (ILV), and heart rate (HR) during modulation of the autonomic nervous system (see [1] and ref. therein). Using a transfer function approach based on spectral analysis, it has been shown that all the linear filter characteristics (ILV→HR, ILV→BP, BP→HR) were low-pass. In states of sympathetic and parysympathetic activation the computed coherence function $\gamma(f)$ within the frequency range 0 to 0.5 Hz is not close enough to one and precludes the use of linear approximation [1]. Moreover, in some studies the system was assumed to be linear and stationary and calculation of $\gamma(f)$ and transfer function using power spectrum computation resulted in potentially confusing results.

In this report, we propose a nonlinear (NL) approach to characterize the relationship between the sympathetic nerve activity and the mean blood pressure. To this end, we first assessed the following transfer functions on the same stationary time interval: MBP→MSNA, MSNA→MBP. We found that the linear approximation was valid only in the low frequency band (0-0.15 Hz) because the reconstructed time waveforms from the impulse response $h(t)$ associated with the linear transfer function MBP→MSNA only matched the MSNA in this frequency interval. The computed coherence function however showed evidence for the existence of a nonlinear relationship between these signals. We then modelized the nonlinear relation using radial basis functions [2] wich allowed us to compare the reconstructed MSNA obtained both with linear and nonlinear models. We found that this NL model allowed a better approximation of the relationship between MSNA and MBP.

METHOD

General procedure: After providing informed consent, we obtained, in a quietly restling 32 years old subject, simultaneous measurements of heart rate (ECG), respiratory excursions (pneumobelt), blood pressure (Finapres Ohmeda, Englewood), and efferent MSNA [3] which were recorded continuously on an electrostatic recorder and digitized on a 486 intel PC with an A/D board (Labmaster).

MSNA procedure: Multiunit fibre recordings of efferent MSNA were obtained with unipolar tungsten microelectrodes inserted selectively into muscle nerve fascicles of the peroneal nerve posterior to the fibular head by the microneurographic technique of Vallbo et al. [3]. The neural signals were amplified (by 20–50 X 10^3), filtered (700–2000 Hz), rectified and integrated (time constant 0.1s).

Data analysis: All the signals (MBP, ECG and MSNA) were sampled at 500 Hz and acquired during 360 s. The MBP was extracted from the recorded signal by using an anti-aliasing filter followed by a 4th order Butterworth low pass filter with a cut-off frequency of 0.5 Hz. The efferent MSNA signal was processed with linear and nonlinear morphological filters in order to suppress all artifacts and noise. The resulting nerve signal was then post-processed using a sliding integration of 1 s duration throughout the data and the resulting signal was called: IMSNA. Finally, the MBP and IMSNA signals were resampled at 4 Hz using spline interpolation.

RESULTS

Linear modelization: In order to compare the linear approach used by Saul et al. [1], we selected a 96.5 s stationary time interval. We then computed the optimal finite impulse response $h_{opt}(t)$ using the Wiener-Hopf algorithm optimized with the Akaike criteria [4, 5]. A 30 length with 1.5 s delay impulse response was found. The impulse response in Figure 1 shows a non-causal non-symmetric behaviour. The non-causality highlights the fact that IMSNA and MBP influence each other whereas the lack of symmetry indicates that the relationship is non reciprocal: i.e. under baseline conditions bursts of IMSNA occur mainly as a result of variations in MBP.

Finally, the transfer function (frequency response) $H(f)$ of the system MBP→IMSNA was obtained (Figure 1) using only the causal part of $h_{opt}(t)$.

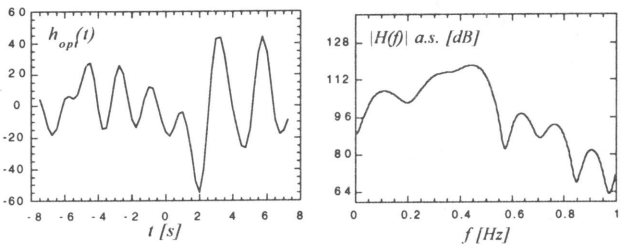

Figure 1

Figure 1 shows that under resting conditions the influence of MBP on IMSNA is stronger compared to the reverse case. The delay of 1.5 s between a change in MBP and the corresponding sympathetic nerve discharge is mainly due to the time it takes for the sympathetic nerve action potentials to travel from the central nervous system to the IMSNA recording site below the knee (the conduction velocity of the sympathetic nerve fibers is approximately 1 m/s; the transmission time from the baroreceptors to the central nervous system is is very short)

The reconstruction of the IMSNA from the MBP gives reliable results in the low frequency band only because the transfer function in Figure 1 has a low pass characteristic (see Figure 3). To make this comparison, the low passed IMSNA (4th order Butterworth filter with cut-off frequency of 0.5 Hz) signal has been generated. Intrinsic bursting properties of the IMSNA are not well reproduced. The quality of the approximation was measured with the following quantity

$$\langle R_{ee} \rangle \equiv \left(\int_{\Omega} R_{ee}(t)dt \right) / \Omega \qquad (1)$$

where $R_{ee}(t)$ stands for the autocorrelation of the error signal $e(t)=IMSNA(t)-Predict\_IMSNA(t)$. With the linear model we obtain $\langle R_{ee} \rangle = 5.1 \times 10^3$.

The coherence function $\gamma(f)$ was estimated using cross-spectral estimation [5]. Figure 2 shows that, within the range of 0 to 0.15 Hz, $\gamma(f)$ is close to 1 and characterized by small coherence values outside this range; this behaviour is typical for a NL system.

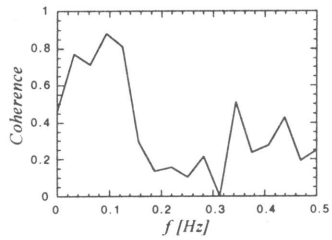

Figure 2

Nonlinear modelization: Among the many possible NL models for this approximation task (Polynomial, Volterra Series, Neural Networks, Radial Basis Functions), we have chosen the radial basis function (RBF) approach. RBF modelization offers the advantage to be rapidely implemented and usually gives accurate results [2]. The RBF model can be considered as a one layer artificial neural network, and therefore linear and purely nonlinear terms cannot be separated. The full specification of the model is given by the following two sets of parameters (p, m) and $\{\lambda_i, c_i, \beta_i\}$ for $i=1,2,...,m$ in case of Gaussian radial basis function $\Phi_i(x, c_i, \beta_i)$. The center of the Gaussian were found with the Loyd algorithm [6], the β_i were computed from variance estimation, the order p was determined with a distortion criteria and the λ_i were computed with a standard LMS algorithm [4, 5]. In our case p=10 and m=20. The reconstructed IMSNA from this NL model is shown in figure 3 and $\langle R_{ee} \rangle = 3.34 \times 10^3$ which is much lower than in the linear case.

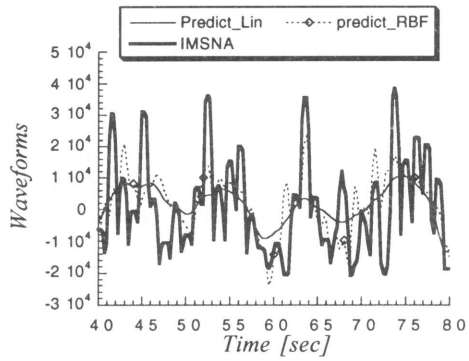

Figure 3

CONCLUSIONS

Using simple signal processing treatments, we were able to show that MBP and MSNA influence each other. However, under resting conditions this relationship is non-reciprocal and it is the MBP which mainly determined MSNA (and not vice versa).

While the linear model allowed us to deduce some interesting properties of the MBP-MSNA interaction (causality and symmetry), the nonlinear model performs better when one considers the reconstruction the MSNA signal as a function of MBP.

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