Cardiovascular Response to Sinusoidal Neck Suction in Healthy Volunteers and Orthostatic Intolerance Patients

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Abstract

The dynamic response to sinusoidal neck suction, of the RR interval, systolic arterial blood pressure and muscle sympathetic nerve activity series, was studied in 10 controls and 5 patients with orthostatic intolerance.

Particularly, by different spectral techniques (autoregressive, short time Fourier transformation), the cardiovascular and MSNA variability was analyzed during 0.1Hz and 0.2Hz frequency of neck suction.

Moreover, using the autoregressive model, a quantitative analysis, of particular power spectral frequency bands, was done. Finally, a chirp neck suction input signal was applied to qualitatively compare the frequency response. The patients with orthostatic intolerance showed a partial blood pressure response to NS, particularly over 0.1 Hz compared to controls.

1. Introduction

Orthostatic intolerance (OI) is commonly defined as a >30 bpm increase in heart rate (HR) upon standing associated with orthostatic symptoms but without significant orthostatic hypotension [1,2,12]. The pathophysiology of this disorder, which mainly affects women in the second or third decade of life, is understood imperfectly. The unifying feature found in patients with OI is the presence of symptoms suggestive of cerebral hypoperfusion (eg, presyncope, visual changes, altered mentation) associated with standing despite largely sustained systemic arterial pressure.

Neck suction (NS) procedures have been widely used to evaluate the carotid sinus baroreflex function in humans [3-5]. During NS, negative pressure is applied around the neck to active the carotid sinus baroreflex, resulting in a decrease in arterial pressure. Spectral analysis techniques are used to characterize different cardiovascular, neuronal, and respiratory fluctuations [5-10,12].

This technique allows for evaluation of synchronism and modulation of the cardiovascular series and muscle sympathetic nerve activity (MSNA) and thus tests the ability of the arterial baroreflex to respond to NS stimulation at different frequencies in separate parts of the baroreflex loop.

2. Methods

2.1. Data acquisition

Data have been collected at the Vanderbilt University Autonomic Dysfunction Center and at the Department of Internal Medicine of the University of Milan. The study included 10 controls and 5 patients with OI. Before beginning the examination full written consent was obtained and the maneuvers required were explained.

The following signals were continuously recorded on a computer by a 14-bit analog-to-digital converter (Windaq DI-220 system, 500 Hz of sampling frequency): electrocardiogram (lead II), respiration (by a strain gauge thoracic belt), blood pressure (Finapres, Ohmeda 2300), MSNA.

Sympathetic nerve recordings. Postganglionic muscle sympathetic nerve activity was recorded with standard microneurographic techniques [2,11,12]. A tungsten microelectrode was inserted into the peroneal nerve near the popliteal fossa of the right leg and positioned in the sympathetic fibers. The neurograms were measured with a nerve traffic analysis system (662C-3, Bioengineering of University of Iowa, Iowa). The raw neurogram amplified (factor of 999x100), filtered with the bandpass filter (700 Hz to 2 kHz), rectified, and integrated with a time constant of 0.1s to obtain a mean voltage neurogram. Assessment of the correct position in the fibers supplying the muscle was made by observing typical heart-period related spikes and increased burst frequency with end-expiratory breath holds and Valsalva

maneuvers without any responses to a scare or skin stroking.

Baroreceptor stimulation. Neck suction was applied by means of two deformable lead cups joined together by elastic bands and connected with a vacuum cleaner whose power was modulated by a second computer equipped with a 12-bit digital-to-analog board through a phase-control power unit. This computer first generated a sinusoidal function of 0.1Hz and then 0.2Hz for 100 seconds each. After these two steady frequency NS signals, the system generated a frequency changing function (so called "chirp" function) started at the frequency of 0.02Hz for 100 seconds, then continuously increased up to 0.30Hz by 0.02Hz increments for a total 266 seconds. The pressure within the neck oscillated steadily from 0 to –50 mmHg.

2.2. Protocol

At least 15 min were allowed for stabilization in resting supine position then the signals were simultaneously and continuously recorded for 10 min (baseline condition). Respiration was paced at 0.25Hz with the use of visually-acoustic technique, with care being taken to avoid hyperventilation. Within the three sections of NS the respiration was spontaneous for 5 min and started to be controlled 1 min before NS.

2.3. Data analysis

Sympathetic burst were verified and edited by a careful inspection of the integrated neurogram signal. We calculated the area under the burst and convolved it with a low pass filter, then the beat-to-beat area value was multiplied by the RR intervals to obtain an MSNA series which was as independent of RR intervals variability as possible.

Beat-to-beat RR intervals and systolic arterial pressure (SAP) variability series were calculated offline and synchronized with the assumption that the i-th SAP value is contained inside the i-th cardiac cycle.

To qualitatively analyze the cardiovascular and MSNA series for the presence of the rhythms induced by NS input signal, we applied the Short Time Fourier Transformation (STFT):

$$STFT_x(\tau, f) = \int x(t)\, g^*(t-\tau)\, e^{-j2\pi ft}\, dt$$

where g(t) is the window function. Using this time-variant technique we set a 10 sec time increment with a 90 sec window length for the series acquired during chirp NS and a 5 sec time increment with a 50 sec window length for other NS conditions.

The autoregressive model was chosen to evaluate the power content (of RR intervals, SAP and MSNA spectrum) in the two bands of physiological interest (LF: around 0.1Hz; HF: at 0.25Hz and also around 0.2Hz during neck suction at this frequency). The power in the bands of interest has been normalized by the total power and multiplied by 100.

This approach allows us to quantitatively compare the activation in these characteristic bands in the two groups during baseline conditions, 0.1, and 0.2Hz neck suction as shown in Fig. 4.

The differences between controls and patients with OI were evaluated using a Student's t test. A value of $P<0.05$ was considered statistically significant.

3. Results

The cardiovascular response to 0.1Hz NS showed a pronounced increase in power centered around 0.1Hz in RR interval as well in SAP and MSNA spectra, both in controls and OI. Neck suction with a frequency of 0.2Hz induced a significant peak around this frequency of stimulation in the RR intervals and MSNA spectra, moderate or no response in the SAP spectra in controls (Fig 1), and absolutely no response in OI.

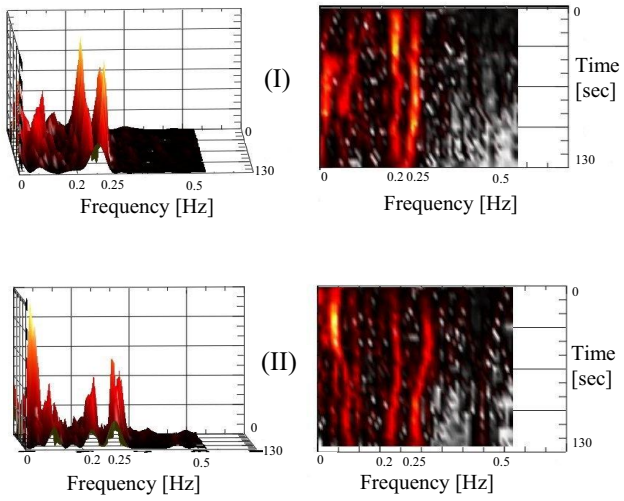

Figure 1. Time variant spectral analysis of RR intervals (I) and SAP (II) series, in one control, during 130 sec of neck suction at 0.2 Hz with control respiration at 0.25Hz. In this case we observed a clear SAP modulation around 0.2Hz. Left panel shows 3 dimensional spectra. Right panel represent two dimensional intensity plot (spectrogram).

Since controls and OI exhibited a similar response to 0.1 Hz NS but differed during 0.2 Hz NS, we want to find the exact frequency at which the response of the healthy subjects differs from that of the OI patients using

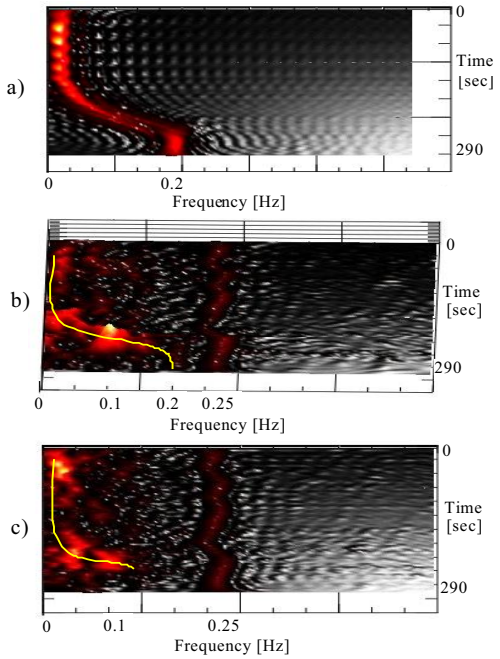

Figure 2. STFT of (a) NS input signal, (b) RR intervals and (c) SAP series, during chirp (0.02-0.2Hz) NS in a control.

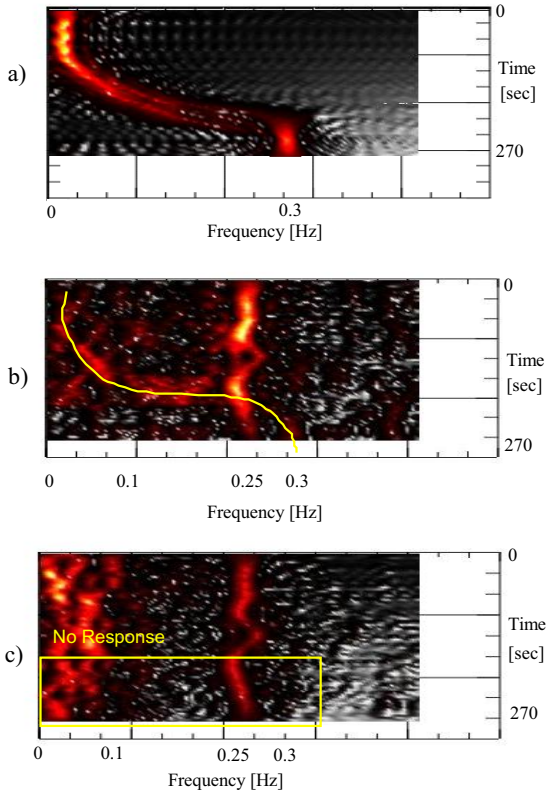

Figure 3. STFT of (a) NS input signal, (b) RR and (c) SAP series, during chirp (0.02-0.3Hz) NS in OI.

chirp NS stimulation. Using frequency domain analysis we found that the two populations differ in the response of SAP variability to chirp NS while response of RR intervals variability was identical. In controls, SAP could follow NS stimulations up to 0.14-0.16Hz, however OI SAP response was detectable only at frequencies below 0.08Hz (Fig 2-3).

Analyzing the mean response to 0.1Hz NS in the two groups with the AR model, we observed no significant differences in the LF power spectral density during NS in RR intervals and SAP series. However, there was a significant increase in the LF power during 0.1Hz NS compared to baseline conditions in controls, but no such change in OI was observed (Fig 4). During 0.2Hz NS we noticed an important activation around this frequency in the RR intervals (significant higher in controls than in OI) and only a partial activation in the SAP (absent in the OI). It is also interesting to note the significantly lower power of SAP variability in HF band of the OI patients. AR analysis the MSNA response revealed a significant difference between controls and OI at 0.2 Hz NS.

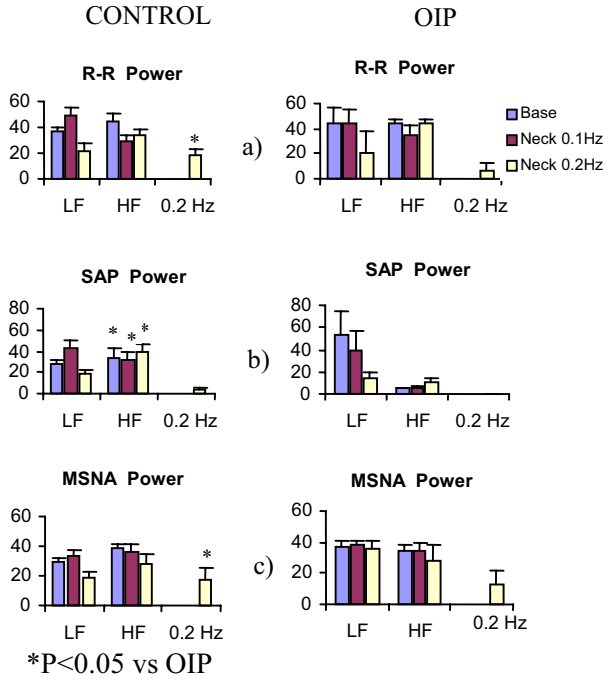

Figure 4. Spectral decomposition (in LF, HF and 0.2Hz band), by AR model, of RR intervals, SAP, and MSNA (a, b, c) in controls and OI during base condition, 0.1Hz and 0.2Hz NS.

4. Discussion and conclusions

In this study, we demonstrated the usefulness of combining a qualitative time-frequency display with a quantitative analysis using an AR model. The modulation of the carotid baroreceptors induced corresponding RR

interval oscillations in the whole frequency range from 0.02 to 0.30Hz in both controls and OI demonstrates the ability of the heart to follow high frequency of baroreceptor stimulations. However, we found more pronounced response at high frequency NS stimulation in controls than compared to OI. The absent of increase of power in the LF band in RR intervals and SAP series during 0.1Hz NS compared to baseline, could be due to an already high LF modulation in resting conditions. A lower corner frequency of SAP response to baroreceptor stimulation was detected in OI, suggesting changes in neuro-mechanical coupling properties. The analysis of the dynamic response to sinusoidal neck suction is a useful diagnostic tool in patients with orthostatic intolerance.

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