# Autonomic Nervous System Non-stationary Response to Controlled Changes in Barometric Pressure

Carlos Sánchez<sup>1,2,3</sup>, Mariola Peláez-Coca<sup>1,2</sup>, M<sup>a</sup> Teresa Lozano<sup>1,4</sup>, Montserrat Aiger<sup>1</sup>, Alberto Hernando<sup>1,2</sup>, Eduardo Gil<sup>2,3</sup>

<sup>1</sup> Centro Universitario de la Defensa (CUD), Zaragoza, Spain

<sup>2</sup> BSICoS Group, Aragón Inst. of Engineering Research (I3A), IIS Aragón, University of Zaragoza

<sup>3</sup> CIBER-BBN, Zaragoza, Spain

<sup>4</sup> RoPeRT Group, Aragón Institute of Engineering Research (I3A), Zaragoza, Spain

#### Abstract

Autonomic Nervous System (ANS) controls a number of bodily functions, such as the heart rate (HR). However, the ANS response is strongly dependent on the surrounding environment. In particular, changes in barometric pressure have important effects on ANS response, but they are difficult to assess in extreme conditions such as a hyperbaric environment. The main goal of this study was to evaluate the dependence of indices related to the ANS response derived from the electrocardiographic signal (ECG) with barometric pressure. In order to do that, a database consisting of ECG recordings of 30 subjects who were introduced into a hyperbaric chamber was used. The analysed indices were derived from the heart rate variability signal: the power of the low-frequency band ( $P_{LF}$ : 0.04 - 0.15 Hz), the power of the high-frequency band ( $P_{HF}$ : 0.15 - 0.4 Hz), the ratio of instantaneous  $P_{LF}$  with respect to the sum of instantaneous  $P_{LF}$  and instantaneous  $P_{HF}$ , and the ratio of instantaneous  $P_{LF}$  with respect to instantaneous  $P_{HF}$ . High inter-subject variability was observed in the results, but significant differences were found in both  $P_{LF}$  and  $P_{HF}$  when pressure gradually increased to 5 atm (initial phase) and then decreased (final phase) with respect to the baseline. Changes in the power ratios were not so significant in general.

### 1. Introduction

Human intrinsic curiosity has made us push our body to limits that it is not totally prepared to face. For example, diving is a common activity many people do that can be dangerous if it is not performed in a controlled manner. Water density is considerably higher than air ( $\sim$ 800 times), so a descent of 10 m in water supposes an increase in barometric pressure of 1 atm. Because of that, recreational diving is limited to 40 m, although professional divers may go deeper.

Among others, an important factor to take into account during diving is the change in partial gas concentration that occurs at higher pressures. This may eventually cause decompression sickness, with severe associated health problems, if the changes in pressure are not performed gradually. Hydrostatic pressure increases with depth, resulting in changes in cardiac pumping: increase in the systolic volume and heart rate (HR) reduction in order to maintain an adequate cardiac output minimizing the impact on the body [1]. This adaptation is possible thanks to the response of the Autonomic Nervous System (ANS). However, due to the implicit difficulties of deep immersions, assessment of the response of the ANS to large changes in pressure is challenging. Studies aiming at monitoring and controlling this response under these extreme conditions may be interesting to divers, for example in the training of military personnel.

In this study, we extracted the heart rate variability (HRV) from the electrocardiographic signal (ECG) to evaluate the response of the ANS, since it can be derived from frequential indices of HRV [2]. Our main goal was to characterize the dependence of indices related to both branches of the ANS, sympathetic and parasympathetic, on barometric pressure using a hyperbaric chamber. In order to perform this analysis, ECG signals were recorded for 30 subjects during a protocol of increasing pressure, mimicking descent to 40 m under water, followed by a gradual decrease, mimicking ascent back to water surface.

## 2. Materials and methods

# 2.1. Database

The complete database used in this study consisted of 30 volunteers (26 males and 4 females) with ages ranging from 21 to 44 years old (mean  $28.93 \pm 6.42$ ). A significant

percentage of these volunteers were military personnel (22 of 30; 73% of the subjects). Five of the subjects were discarded due to either highly artifacted signals, leading to non-physiological values of the indices described in the following sections, or incomplete recordings due to failures in the device and/or the electrodes attachments to the skin. All the volunteers gave written consent validated by the Ethics Committee.

The device used for ECG recording was Nautilus, developed by the University of Kaunas, Lithuania [3]. This device allowed us to record the ECG signal with three non-orthogonal leads at a sampling frequency of 2000 Hz. After the recordings, signals were processed using MATLAB.

The protocol inside the hyperbaric chamber had a duration of about 2 hours and consisted of four stages, whose durations were in agreement with the decompression table recommendations (see *www.naui.org/resources/*):

1. Initial baseline at 0 m (i.e. 1 atm; subjects relax for  $\sim$ 20 min before immersion).

2. Descent from 0 to 40 m (i.e. from 1 to 5 atm; duration  $\sim$ 30 min).

3. Ascent from 40 to 20 m (i.e. from 5 to 3 atm; duration  $\sim$ 10 min).

4. Ascent from 20 to 0 m (i.e. from 3 to 1 atm; duration  $\sim$ 60 min).

### 2.2. Heart rate variability signal

First of all, delineation of the recorded ECG signal to detect the position of the heart beats was performed using an algorithm based on the wavelet transform [4]. Ectopic beats, missed beats and false detections were identified with the same algorithm [5]. Then, the HR series sampled at 4 Hz,  $d_{\text{HR}}(n)$ , was obtained using the integral pulse frequency modulation model (IPFM) [5,6].

$$d_{\rm HR}(n) = \frac{1 + \mathfrak{m}(n)}{T(n)},\tag{1}$$

where  $\mathfrak{M}(n)$  represents the modulating signal, which carries the information from ANS, and T(n) is the mean heart period, which is considered to be slow-time-variant by this model.

A time-varying mean HR,  $d_{\text{HRM}}(n)$ , was obtained by low-pass filtering  $d_{\text{HR}}(n)$ , with a cutoff frequency of 0.03 Hz:

$$d_{\rm HRM}(n) = \frac{1}{T(n)}.$$
 (2)

The HRV signal was estimated as in [6]:

$$d_{\rm HRV}(n) = d_{\rm HR}(n) - d_{\rm HRM}(n). \tag{3}$$

Finally, the modulating signal was computed as follows:

$$\mathfrak{m}(n) = \frac{d_{\mathrm{HRV}}(n)}{d_{\mathrm{HRM}}(n)}.$$
(4)

### 2.3. Frequency indices

Time-frequency analysis was applied over  $\mathfrak{m}(n)$  to characterize the fast response of the ANS to barometric changes. In order to perform this analysis, the SPWVD was selected because it provides better resolution than nonparametric linear methods, independent control of time and frequency filtering, and power estimates with lower variance than parametric methods when rapid changes occur. The SPWVD was calculated as shown in equation (5). The analytic signal  $a_{\mathfrak{M}}(n)$  is defined as  $a_{\mathfrak{M}}(n) =$  $\mathfrak{m}(n) + j \cdot \mathfrak{m}(n)$ , where  $\mathfrak{m}(n)$  represents the Hilbert transform of  $\mathfrak{m}(n)$ . The terms g(n) and h(l) are time and frequency smoothing windows, chosen to be Hamming windows whose lengths are  $2 \cdot N + 1 = 203$  and  $2 \cdot L + 1 = 1025$ samples, respectively [7].

In order to observe the dependence of the ANS with barometric pressure during the four immersion stages, the recorded ECG signals were divided into segments of 100 s duration for the computation and averaging of four classic indices from the SPWVD:

- $P_{\text{LF}}$ : power in the LF band (0.04 0.15 Hz).
- $P_{\text{HF}}$ : power in the HF band (0.15 0.4 Hz).

•  $P_{\text{LF}n}$ : instantaneous power in the LF band over the sum of the instantaneous powers of both LF and HF bands.  $P_{\text{LF}n} = P_{\text{LF}}/(P_{\text{LF}} + P_{\text{HF}})$ 

•  $R_{\rm LF/HF}$ : ratio between the instantaneous power in the LF band and the instantaneous power in the HF band.  $R_{\rm LF/HF} = P_{\rm LF}/P_{\rm HF}$ 

Figure 1 shows an example of a time-frequency map for one subject  $(P_{\mathfrak{M}}(n, m))$  with the two bands of interest delimited: Low Frequency (LF: 0.04 - 0.15 Hz) and High Frequency (HF: 0.15 - 0.4 Hz).



Figure 1: Time-frequency map of one of the subjects at 5 atm with LF and HF bands delimited by dotted black and solid red lines, respectively.

$$P_{\mathfrak{M}}(n,m) = 2 \cdot \sum_{l=-L+1}^{L-1} |h(l)|^2 \cdot \left[ \sum_{n'=-N+1}^{N-1} g(n') a_{\mathfrak{M}}(n+n'+l) a_{\mathfrak{M}}^*(n+n'-l) \right] \cdot e^{-j2l(m/M)\pi},$$

$$m = -M + 1...M.$$
(5)

# 2.4. Outliers removal and statistical analysis

In order to identify extreme outliers, the interquartile range  $(IQR = Q_3 - Q_1)$  for each index was calculated. Subjects whose indices,  $M_x$ , were out of the following limits were identified and removed from posterior analysis:

$$low M_x = Q_1(M_x^{i=1..N_s}) - \delta \cdot IQR(M_x^{i=1..N_s}), \quad (6)$$
  
$$high M_x = Q_3(M_x^{i=1..N_s}) + \delta \cdot IQR(M_x^{i=1..N_s}), \quad (7)$$

where  $N_s$  is the number of subjects and delta = 3. Furthermore, respiration frequency, estimated from the ECG signals as in [8], was used to discard subjects that presented an abnormally low respiratory frequency (<0.15 Hz, coincident with the boundary between LF and HF bands) to avoid misinterpretation of the ANS response.

A statistical analysis of the four frequency indices was then performed in order to assess statistical significance of the results. The Shapiro-Wilk test was applied to check statistical normality of the indices. Then, if the distribution was normal, the Student's t-test was applied, whereas if the distribution was not normal, the Wilcoxon signed-rank test for paired samples was used. A *p*-value  $\leq 0.05$  denotes significant differences between distributions.

These tests were applied to each one of the four indices extracted from the HRV signal for particular values of barometric pressure during the different stages of immersion with respect to the distribution at the initial baseline pressure (1 atm).

### 3. Results

As shown in Figure 2, significant differences in the power of the HRV classical bands ( $P_{\rm LF}$  and  $P_{\rm HF}$ ) have been found for most values of pressure during the immersion protocol with respect to the initial values at 1 atm. Interestingly, there is an increasing trend in the median values for both  $P_{\rm LF}$  and  $P_{\rm HF}$ , although the inter-subject variability becomes also higher, particularly in  $P_{\rm HF}$ . An increase in  $P_{\rm LF}$  is related to the activation of the sympathetic system, which occurs when the subject is exposed to various types of stressors [9,10]. The results in this study show a significant increase in  $P_{\rm LF}$  immediately after the immersion starts (from 1 to 1.5 atm), whereas the changes in  $P_{\rm LF}$  are less prominent as the immersion progresses. Similarly,  $P_{\rm HF}$ .

mainly reflecting parasympathetic activity [2], shows a notable initial increase at 1.5 atm followed by slight increments until maximum depth (5 atm) is reached, in agreement with previous studies [11]. The ratios  $P_{\rm LFn}$  and  $R_{\rm LF/HF}$ , reflecting sympathetic dominance and sympathovagal balance, respectively [2], also show an increasing tendency when pressure increases. However, their variations with respect to the measurements at 1 atm are less notable than those of  $P_{\rm LF}$  and  $P_{\rm HF}$ , only showing statistical significance at very high pressures.

#### 3.1. Limitations

In this study we focused on changes in indices related to the ANS response at specific barometric pressures. Nevertheless, the long time spent in the hyperbaric chamber ( $\sim$ 2 hours) may also play an important role in the body adaptation to pressure variations.

Removal of signal segments with low respiratory frequency may affect the comparison between the distributions of values of powers and ratios. There can be subjects able to breath slowly at rest (1 atm), whose initial measurements are discarded, but not after the immersion starts. Complete elimination of the influence of respiration on the LF band is however a challenging task.

### 4. Conclusions

Frequency domain HRV indices allow us to differentiate between the different stages during immersion. Both LF power and HF power increase when more time is spent at higher pressures than normal. Increments of pressure also entail slight increases in the sympathovagal balance evaluated through the relationship between the powers in LF and HF bands. Observation of these indices may help in the identification of hyperbaric environments. Timebased parameters and respiration signal could be used in further studies since its analysis would add valuable information to characterize body response to changes in barometric pressure.

#### Acknowledgements

This work has been partially financed by Ministerio de Economía, Industria y Competitividad, FEDER, DGA and Centro Universitario de la Defensa through the projects TEC2014-54143-P, TIN2014-53567-R, DGA T04-FSE, CUD2013-11, CUD2016-18 and UZCUD2016-TEC-03.



Figure 2: Boxplots, representing the median and variability in the 25 subjects, of the four frequency indices:  $P_{\rm LF}$ ,  $P_{\rm HF}$ ,  $P_{\rm LF_n}$ , and  $R_{\rm LF/HF}$ , for barometric pressures between initial 1 atm, 5 atm, and final 1 atm. Distributions of indices displayed every 0.5 atm (\* $p \le 0.05$ )

The authors would like to thank Hospital General de la Defensa de Zaragoza, Regimiento de Pontoneros y Especialidades de Ingenieros nº 12 for their valuable collaboration, and the algorithms facilitated by the consolidated research group BSICoS.

### References

- Widmaier EM, Raff H, Strang KT. Vander's Human Physiology. The Mechanisms of Body Function. Boston: McGraw-Hill Higher Education, 2008.
- [2] TFESC, NASPE. Heart Rate Variability: Standards of Measurement, Physiological Interpretation, and Clinical Use, 1996.
- [3] Sokas D, Gailius M, Marozas V. Diver physiology monitor and its graphical user interface. In Proceedings of International Scientific - Practical Conference, Virtual Instruments in Biomedicine. 2016; 5–9.
- [4] Martínez JP, Almeida R, Olmos S, Rocha A, Laguna P. A wavelet-based ECG delineator: evaluation on standard databases. Biomedical Engineering IEEE Transactions on April 2004;51(4):570–581.
- [5] Mateo J, Laguna P. Analysis of heart rate variability in the presence of ectopic beats using the heart timing signal. IEEE Trans Biomed Eng 2003;50(3):334–343.
- [6] Bailón R, Laouini G, Grao C, Orini M, Laguna P, Meste O. The integral pulse frequency modulation model with timevarying threshold: Application to heart rate variability analysis during exercise stress testing. Biomedical Engineering IEEE Transactions on March 2011;58(3):642–652.

- [7] Bailón R, Garatachea N, de la Iglesia I, Casajús J, Laguna P. Influence of running stride frequency in heart rate variability analysis during treadmill exercise testing. Biomedical Engineering IEEE Transactions on July 2013;60(7):1796– 1805.
- [8] Lázaro J, Alcaine A, Romero D, Gil E, Laguna P, Pueyo E, Bailón R. Electrocardiogram derived respiratory rate from QRS slopes and R-wave angle. Annals of Biomedical Engineering October 2014;42(10):2072–2083.
- [9] Berntson GG, Cacioppo JT, Fieldstone A. Illusions, arithmetic, and the bidirectional modulation of vagal control of the heart. Biological Psychology 1996;44:1–17.
- [10] Hernando A, Lazaro J, Gil E, Arza Valdes A, Garzon-Rey J, Lopez-Anton R, de la Camara C, Laguna P, Aguilo J, Bailón R. Inclusion of respiratory frequency information in heart rate variability analysis for stress assessment. IEEE Journal of Biomedical and Health Informatics 2016;1–1.
- [11] Lund V, Kentala E, Scheinin H, Klossner J, Sariola-Heinonen K, Jalonen J. Hyperbaric oxygen increases parasympathetic activity in professional divers. Acta Physiologica Scandinavica September 2000;170(1):39–44.

Address for correspondence:

Carlos Sánchez Tapia Centro Universitario de la Defensa (CUD) Academia General Militar (AGM) Ctra. Huesca s/n, 50090 Zaragoza, Spain. cstapia@unizar.es