Heart rate variability as a predictor of hypobaric hypoxia in aircraft pilots

Variabilidad de la frecuencia cardíaca como predictor de hipoxia hipobárica en pilotos de aviones

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Abstract

Background: early recognition of hypoxia may decrease aviation accidents happening due to human error and measurement of heart rate variability can be a tool to detect hypoxic events. We aim to determine if heart rate variability relates to hypoxia exposure in subjects who carried out hypobaric chamber training.

Methods: we studied 44 pilots during hypobaric hypoxia. Oxygen saturation, time of exposure to hypoxia and heart rate variability were measured in the three phases of flight: denitrogenation, hypoxia and descent to ground and analyzed through an autoregressive model, and a fast fourier transform for high frequency, low frequency and the low frequency/high frequency ratio.

Results: population was composed of 44 Colombian Air Force male pilots, 42 males and 2 females, between the ages of 20 and 40, with a median age of 27.5 years. The power of high frequency and low frequency decreased from denitrogenation to hypoxia and increased from hypoxia to descent to ground. The low frequency/high frequency ratio increased during the whole experiment in fast fourier transform. The autoregressive model failed to show statistical significance for high frequency from hypoxia to descent to ground and for the low frequency/high frequency ratio from denitrogenation to hypoxia.

Conclusion: hypoxia leads to changes in the autonomous nervous system balance that can be assessed through heart rate variability. More studies are needed to quantify the impact of heart rate variability on decision-making ability and accident prevention in the aviation field.

Keywords: Heart rate; Variability; Hypoxia; Pilots.

Resumen

Introducción: el reconocimiento temprano de la hipoxia puede disminuir los accidentes de aviación que ocurren debido a errores humanos y la medición de la variabilidad de la frecuencia cardíaca puede ser una herramienta para detectar eventos hipóxicos. Nuestro objetivo es determinar si la variabilidad de la frecuencia cardíaca se relaciona con la exposición a la hipoxia en sujetos que realizaron entrenamiento en la cámara hipobárica.

Métodos: estudiamos 44 pilotos durante hipoxia hipobárica. La saturación de oxígeno, el tiempo de exposición a la hipoxia y la variabilidad de la frecuencia cardíaca se midieron en las tres fases del vuelo: desnitrogenación, hipoxia y descenso a tierra y se analizaron mediante un modelo autorregresivo y una transformada rápida de Fourier para alta frecuencia, baja frecuencia y baja frecuencia / alta frecuencia.

Resultados: la población estuvo compuesta por 44 pilotos de la Fuerza Aérea Colombiana, 42 hombres y 2 mujeres, entre 20 y 40 años, con una mediana de edad de 27,5 años. El poder de las frecuencias altas y bajas disminuyó de la desnitrogenación a la hipoxia y aumentó de la hipoxia al descenso al suelo. La relación de baja frecuencia / alta frecuencia aumentó durante todo el experimento en la transformada rápida de Fourier. El modelo autorregresivo no mostró significación estadística para la alta frecuencia desde la hipoxia hasta el descenso al suelo y para la relación de baja frecuencia / alta frecuencia desde la desnitrogenación hasta la hipoxia.

Conclusión: la hipoxia provoca cambios en el equilibrio del sistema nervioso autónomo que pueden evaluarse mediante la variabilidad de la frecuencia cardíaca. Se necesitan más estudios para cuantificar el impacto de la variabilidad de la frecuencia cardíaca en la capacidad de toma de decisiones y la prevención de accidentes en el campo de la aviación.

Palabras clave: frecuencia cardiaca; variabilidad; hipoxia; pilotos.

Introduction

The early recognition of hypoxic hypoxia is becoming a relevant topic in the scientific field, aiming to decrease or even avoid aviation accidents (1) . Pilots are continuously exposed to acute changes in altitude and partial pressure of oxygen, yielding them vulnerable to human error due to hypoxia. (2) . Within the field of aviation, the human factor or "human error" has been a matter of research during the last few decades, and is considered to be the cause of about 75% of aviation accidents (4). Human error may be classified within two categories: decreased performance due to a decline in acquired skills (2) or due to decreased situational awareness (5). Hypoxic hypoxia could be categorized within the second group, due to depletion of time of useful consciousness (TUG), which may lead to impaired judgment and poor decision-making (6).

Heart rate variability (HRV) is described as the variation in the time interval between heartbeats within a previously defined timeframe (6). From the standpoint of physiology, the HRV has the function of adjusting the blood flow and perfusion of different organs, particularly the brain.(5-7) The main methods for studying the HRV may be described through several domains: time, frequency, geometric methods, and non-linear variables. (8)

Changes in the autonomic nervous system (ANS) are characterized by an increase in sympathetic activity, due to an altered density of beta-adrenergic cardiac receptors, conducive to decreased maximal heart rate despite the increase in catecholamine concentration (9). This autonomic cardiac modulation is seen in response to hypoxia in healthy young adults, and seems to depend on the altitude, time of exposure, rate of climb or descent, interindividual variation, fraction of inspired oxygen, physical conditioning, body composition and barometric pressure (10). Thus, HRV could be used as a tool to timely identify pilots who are prone to develop hypoxia-related symptoms such as a reduced cognitive performance and a decreased TUG. Therefore, an objective tool allowing for aircrew members to promptly identify signs and symptoms of hypoxic hypoxia is necessary. Thus, this study aims to describe changes in HRV with hypobaric hypoxia, in a sample composed by the Colombian Air Force flight staff being trained in hypobaric chambers in the Aerospace Medicine Center.

Methods

This is a quasi-experimental and cross-sectional study with 44 pilot subjects who underwent hypobaric chamber training during the second semester of 2018 in the Colombian Air Force Aerospace Medicine Center were included in this study.

Eligibility criteria

The inclusion criteria included aircrew members from Bogota, male and female pilots undergoing high-altitude chamber retraining, who had a valid psychophysical fitness certificate and who were non-smokers. Individuals with a past medical history remarkable for decompression sickness, infectious disease, orthopedic limitations, anemic syndrome, systemic hypertension and those not willing to participate in the study were excluded.

Flight protocol

The pilots entered the altitude chamber , the interbeat interval (RR) was monitored for each individual through a heart rate monitor (Brand: Polar®, Reference: V800, Finland). Then, the helmet and mask were adjusted in order to begin the hypoxic hypoxia training in hypobaric conditions. The PaO2 of each individual was measured during the experiment. This protocol consisted of an initial denitrogenation (DNT) phase for 30 minutes, accomplished through inhalation of 100% oxygen in order to eliminate 50% of blood nitrogen, decreasing the risk of decompression sickness. Once the denitrogenation phase ended, we conducted an ascent to 3,962 meters as a means for verifying ears and paranasal sinuses, so that we could prevent dysbarism. Then, the ascent to 7620 meters was attained through a rate of 610 meters per minute. Once this altitude was achieved, the oxygen mask was withdrawn in order to allow exposure to hypoxic hypobaric hypoxia (HX), which corresponded to the second phase of flight.

Subjects solved a standardized cognitive test under supervision from the on-board trainer, simultaneously , the subjects had to proceed with the recognition and recovery phase aided by an oxygen mask. In cases where this was not possible, the on-board trainer carried out the subject's recovery procedure with 100% oxygen. After this exercise, the descent to ground level (DT) phase began, corresponding to the third phase of flight, at a rate of 610 meters per minute. ending the exercise with the post-flight recommendations.

Heart rate and oxygen saturation record

The Polar® V800 was used for all measurements and for keeping the records on heart rate variability, since it allows to measure R-R interbeat intervals within a predefined time frame. The records were uploaded to the computer with a USB 2.0 port through the polar protrainer 5TM software. Then, an off-line analysis was conducted with the Kubios HRV program (version 2.2 of 2016). The preprocessing of the signal was conducted through a visual observation of the tachogram. Signals with noise levels greater than 3 standard deviations were filtered with the Kubios Very Low filter function. Then, the first 10 minutes of signal were selected for analysis within each phase of flight denitrogenation (DNT), hypoxia and DT. The Kubios software provides data on power in RMS values (ms2) as well as through percentages (%) for the frequency bands between 0.15 - 0.4 Hz, which corresponds to the high frequencies (HF) related to sympathetic activity and frequencies between 0.04 - 0.15 Hz , which corresponds to the low frequencies (LF) related to a modulation of the parasympathetic on the sympathetic. The techniques used by Kubios to obtain power in a frequency band include auto regressive modeling (AR) and the fast fourier transform (FFT). The oxygen saturation percentage data were obtained from a pulse oximeter (Brand: Nonin® Reference: Onix II, USA) considering the recognition of hypoxia symptoms up to 15 seconds after oxygen supplementation began. Time of exposure to hypoxia was measured in minutes by the digital stopwatch of the hypobaric chamber. The initial time stamp corresponds to the moment when the 7620 meters mark was reached and the crewmen removed their oxygen masks. The final time stamp was defined by the moment of recognition and recovery from hypoxia after putting the oxygen mask on again.

Statistical analysis

In the first phase, a univariate analysis was performed, categorical variables were analyzed using frequencies, and quantitative continuous variables were expressed as the median and interquartile range (IQR). Normality was assessed through the Shapiro Wilks test, yielding non-normal distribution. In the bivariate analysis we compared the values of HF, LF and the LF/HF ratio with each moment of the experiment (DNT, hypoxia and DT), as shown on the results. Then, on a third phase, a multivariate analysis was performed through linear regression models to compare the power of HF, LF and the LF/HF ratio from DNT to HPX, hypoxia DT and DNT to DT. Models were adjusted by age, weight, height, body water content, body fat percentage and lean muscle mass. Pairwise comparisons were adjusted by Bonferroni. A p value of <0.05 was set to reject the null hypothesis. All analyses were performed using R version 4.0.1.

Ethical considerations

The study protocol was approved in advance by the Institutional Ethics Committee at the Hospital Militar Central de Bogotá, Colombia. Each subject provided written informed consent before participating.

Results

The sample was composed of 44 Colombian Air Force male pilots, 42 males and 2 females, between the ages of 20 and 40, with a median age of 27.5 years, who were from Bogotá (Colombia) at an altitude of 2.600 meters. The median for the lean muscle mass, body fat percentage and body Mass Index were found to be within normal ranges table 1.

Median values of HF and LF were found to be lower in hypoxia, reaching higher values in DT and DNT, respectively, in both the FFT and AR model Table 2. As for the LF/HF ratio, median values were higher in DT than hypoxia, and LF/HF values were also higher in hypoxia when compared to DNT.

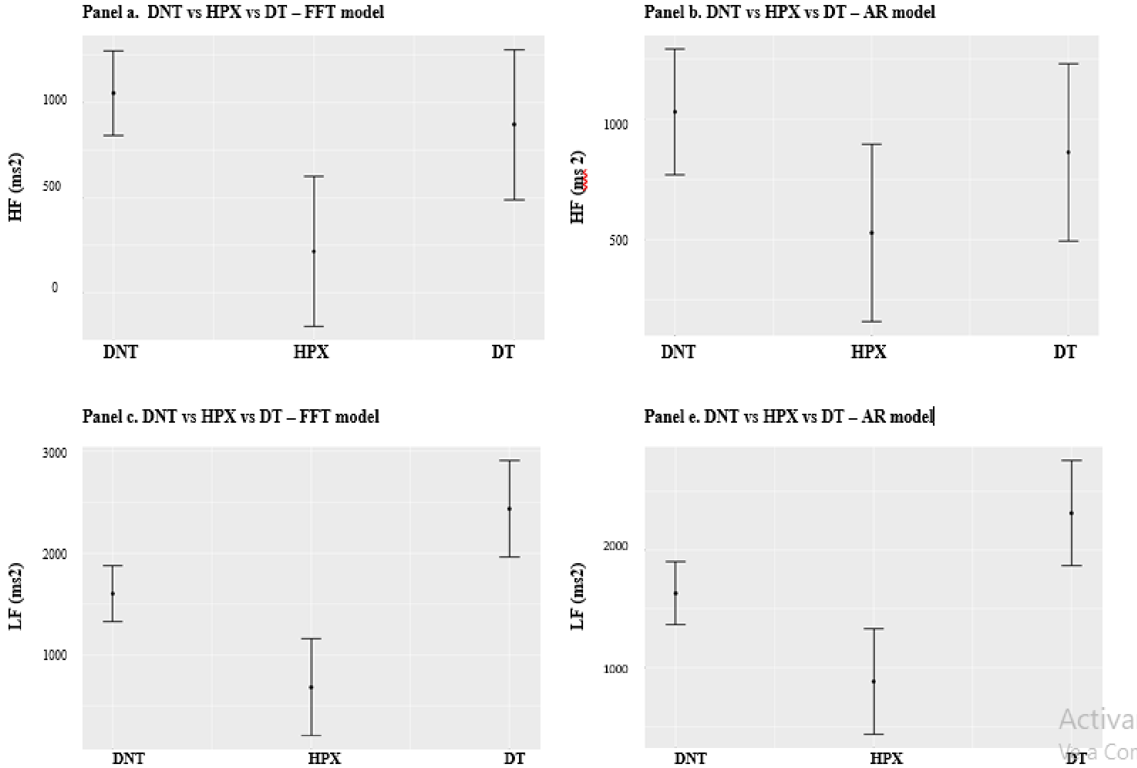
Changes can be found regarding a decrease of the values of the power for HF and LF in both models after exposure to hypoxia from DNT to hypoxia. On the other hand, an increase of HF and LF was observed from hypoxiato DT in the FFT model when pilots were exposed to normoxia from hypoxiato DT, but the AR model failed to reach statistical significance for this comparison in HF table 3. When DNT was compared to DT in both the FFT and AR models, higher values were found in LF, and on the contrary lower values were found in HF but the analysis failed to show statistical significance.

As for the HF/LF ratio, values increased from DNT to hypoxia in the FFT model, displaying a proportional increase of LF compared to HF after the exposure to hypoxia; interestingly, these changes were not observed in the AR model. the values of the LF/HF ratio increased from hypoxiato DT.

For HF, higher values of HF were observed in DNT, and values decreased when subjects were exposed to hypoxia in the FFT model (Panel a) but failed to show a statistically significant difference in the AR model (panel b) Figure 1. Subsequently, DT is related to an increased value of HF in both FFT Figure 1 Panel a and AR Figure 1 Panel b. The power of LF decreased from DNT to hypoxia, and increased from hypoxia DT Statistical significance was attained in both models Figure 2 Panel c and e.

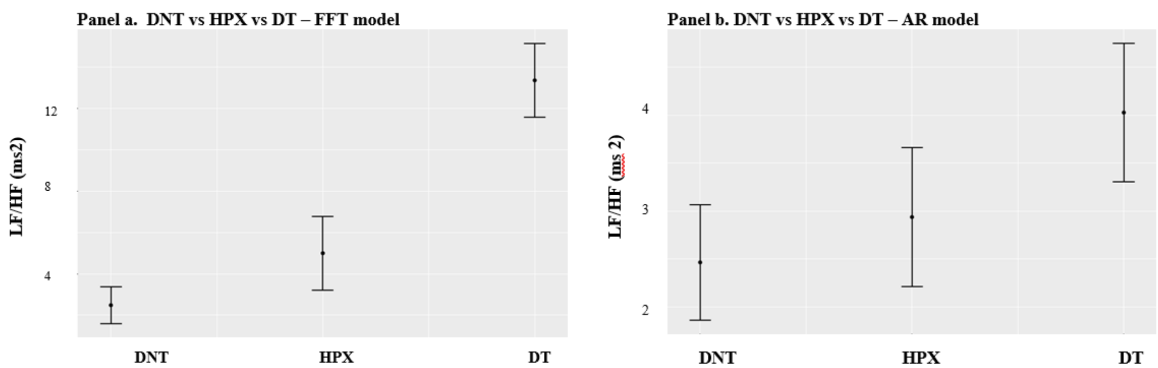
The LF/HF ratio increased progressively from DNT to HPX, and from hypoxia to DT, in the FFT model. Although LF/HF failed to show statistical significance from DNT to HPX, it was significant from hypoxia to DT ($p<0,001$), as evidenced in Figure 2.

Figure 1. HF and LF values in denitrogenation vs hypoxia vs descent to ground.



Notes: LF, Low frequency; HF, high frequency ratio; DNT, denitrogenation phase ; DT, to the descent to ground level; HPX, hypoxia; AR, auto regressive modeling ; FFT, fast fourier transform.

Figure 2. LF/HF ratio values during the different moments of the flight.



* LF, Low frequency; HF, high frequency ratio; DNT, denitrogenation phase ; DT, to the descent to ground level; HPX, hypoxia; AR, auto regressive modeling ; FFT, fast fourier transform.

Table 1. Characteristics of the population.	
Variable (n = 44**)**	
Sex (n - %**)**	
Female	2 (4,5)
Male	42 (95,5)
Characteristics of the sample (Median - IQR**)**	
Age (years)	27.5 (24 – 32.25)
Weight (kilograms)	73.5 (68.3-82.9)
Height (Meters)	1.74 (1.69-1.79)
Body Mass Index	24.9 (22.8-26.5)
Body fat percentage	20.7 (17.8-23.9)
Lean muscle mass (kilograms)	58.7 (55.3-62.9)
Body water content (%)	43 (40.5- 46.8)
Oxygen saturation (%)	70 (66.5-73.2)

Notes: n, number; %, porcentage; IQR, interquartile range.

Table 2. Bivariate analysis for heart rate variability for different moments of evaluation.				
Mode	**Power of the different moments of the flight expressed in square milliseconds (ms2)** (Median – IQR)			
Fast Fourier (ms2)	**Denitrogenation**	**Hypoxia**	**Descent to ground**	***P value***
HF	610.9 (428.4- 1051.6)	130.5 (73.2-298)	477.5 (314.4-1117)	<0,001
LF	1384.3 (970.2- 1722)	599.9 (332.8-1016)	2215 (1432.5- 2846.3)	<0,001
LF/HF	1.8 (1.50- 2.91)	3.6 (2.5-6.9)	11.3 (7.6-18.2)	<0,001
Autoregressive (ms2)	**Denitrogenation**	**Hypoxia**	**Descent to ground**	***P value***
LF	643.0 (430.3-1032.7)	389.6 (223.6-535.3)	475.1 (304.8-1120)	<0,001
HF	1419.2 (970.2- 1848.7)	799 (562.7-1200.8)	2078.8 (1420.2-2538)	<0,001
LF/HF	1.91 (1.45-3.0)	2.17 (1.58-3.0)	3.4 (2.0-5.3)	0.006

Notes: LF, Low frequency; HF, high frequency ratio; IQR, interquartile range.

Table 3. Statistical results of the comparison of HF, LF and the LF/HF values in denitrogenation vs hypoxia vs descent to ground.			
Model of the study	**Comparison of the different moments of the flight**		
Fast Fourier (ms2)	**Estimation DNT vs hypoxia (*Adjusted p value*)**	**Estimation hypoxia vs DT (*Adjusted p value*)**	**Estimation DNT vs DT (*Adjusted p value*)**
HF	834 (0.019)	-668 (0.016)	166 (0.001)
LF	920 (0.046)	-1755 (<0.001)	-835 (0.017)
LF/HF	-2.52 (0.080)	-8.36 (<0.001)	-10.88 (<0.001)
Autoregressive model (ms2)	**Estimation DNT vs hypoxia (*Adjusted p value*)**	**Estimation hypoxia vs DT (*Adjusted p value*)**	**Estimation DNT vs DT (*Adjusted p value*)**
HF	503 (0.025)	-335 (0.298)	168 (0.001)
LF	750 (0.014)	-1432 (<0.001)	-683 (0.030)
LF/HF	-0.473 (0.312)	-1.091 (<0.001)	-1.563 (0.008)

Notes: LF, Low frequency; HF, high frequency ratio; DNT, denitrogenation phase ; DT, to the descent to ground level.

Discussion

We conducted a statistical analysis to compare the power (ms2) of HF, LF and the LF/HF ratio during the different moments of the flight. Our study found changes regarding the HRV in HF, LF, and the LF/HF ratio. It prompts us to consider the relevance of the ANS modulation during hypoxic exposures since it may be a contributing factor for aircraft accidents due to human error.

The parasympathetic activity is reflected by changes in the power of HF, while the power of LF is directly related to a modulation of the parasympathetic on the sympathetic branch of the ANS, and in some cases it is also interpreted as a direct sign of sympathetic activity. Therefore, the LF/HF ratio is a result of the interaction between both ANS branches at the different moments of the flight. In our experiment, the hypoxic exposure from DNT to hypoxia exerted a direct influence on the ANS activity, which was evidenced as a decrease in HF and LF values in both models, FFT and AR. This phenomenon could be attributed to a complex interaction between the different mechanisms responsible for the heart rate and blood pressure regulation. (4-9)

Regardless of the physiological explanation, the ultimate response to hypoxia is an increased sympathetic tone that causes the blood pressure to rise until it finally overcomes the new setpoint of the baroreceptors, and it triggers the baroreflex, which leads to an increased parasympathetic tone that modulates the sympathetic branch of the ANS (11). However, there are several contrasting findings in further comparisons between both models. During the restoration of normoxia, which occurred from hypoxiato DT, a significant increase in LF was noted in the two models, and FFT revealed changes in HF that were not evidenced in AR. In addition, the LF/HF ratio increased consistently throughout the whole experiment in both models, which indicates a persistent sympathetic predominance despite an increased parasympathetic modulation. Nonetheless, this change was not reflected in AR from hypoxiato DT (12). We believe that this phenomenon could be explained by a better performance of FFT to detect small changes in the ANS modulation.

The Colombian Air Force (FAC) pilots included in our study were men and women aged between 20 and 40 years, who were adapted to living at an altitude of 2600 masl. Our results are similar to those of Monteze et al. (13), who studied the HRV and arterial blood pressure in a group of 438 male workers of altitude of 20 to 50 years of age. According to their results, subjects who have a better parasympathetic modulation of the cardiovascular response, which was assessed specifically through HF, have a reduced death rate due to any cause, and performed better at work. Similarly, our subjects were adapted to intermediate altitudes, have the same age range, and also displayed changes in HF, which allows us to infer a possible favorable effect of their characteristics on their performance.

Our results are congruent with those previously reported by the literature. For example, Coppel et al. (14), carried out a bibliographic review and found that significant changes in the cardiovascular response usually take place at altitudes above 25,000 feet (15) , however all of the studies described were performed using a starting altitude below 2000 meters, while in our study pilots are acclimatized to 2600 meters. In addition, no other hypobaric chamber is installed at 2438.4 meters as the one of the FAC. As a result, our findings regarding the ANS modulation in the context of a previous acclimatization are unique and this could give our subjects physiological advantages such as a better AND modulation, a more appropriate response of the baroreceptor and an increased tolerance to exercise. Nevertheless, the existing information of the possible effects of altitude conditioning prior to exposure to hypoxia are scarce, and further research is necessary in order to evaluate the possible benefits and disadvantages of such exposure.

In another study performed by the Argentine Air Force, 17 male pilots were exposed to hypobaric hypoxia at 27,000 feet of altitude, and both the sympathetic and parasympathetic activity were found to increase significantly.(16)

Body composition could also play a role in the ANS response, as measured by the HRV. It has been found that a high body fat percentage may be directly associated with a less efficient balance between sympathetic and parasympathetic ANS, which causes lower HRV values with a delayed recovery from a baseline and lower values of the LF/HF ratio (17) . In contrast, lower adipose tissue correlates with a better ANS balance, and an increased lean muscle mass has been linked to higher HRV values, specifically in LF (18). Likewise, cyclic exposures to high altitude, as the ones seen in our subjects, could be of importance because they may lead to a better energetic metabolism causing lower body fat percentages (18). It has also been described that dehydration states correlate with lower LF/HF ratios because of an increased vagal tone, and a relationship between lower HRV values and older ages has been established (19).

The limitations of this study are in the retrospective nature; the number of subjects may not be so large as to allow an association study. In addition, we were unable to find studies that directly addressed the relationship between the previously mentioned factors and HRV during hypobaric hypoxic exposures, neither this variable nor any of the other mentioned seemed to influence the results of our study.

Conclusions

An adequate balance of the autonomic nervous system becomes a factor anticipating the response to hypoxia with a predominance of LF through an acute response mediated by sympathetic activity and predominance of parasympathetic activity through HF after exposure to hypoxia. More studies are needed to quantify the impact of heart rate variability on decision-making ability and accident prevention in the aviation field.

Declaration of Conflicting Interests
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