Gender-Related Differences in Time and Spectral Entropy Rate Measures of Cardiovascular Variability

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***Abstract*—In this work, we investigate gender-related differences in the autonomic regulation of the cardiovascular system using information-theoretic measures of entropy rate (ER) and mutual information rate (MIR) computed in the time- and frequency domains. Analyses were carried out on heart period, systolic and diastolic blood pressure time series extracted on 276 young healthy subjects in the resting supine condition. The results of spectral ER and MIR measures evidenced in females a reduced dynamical cardiovascular complexity and decreased pairwise coupling within the Low Frequency band that can be related to the lower sympathetic activity if compared to males.**

***Index Terms*—complexity, cardiovascular variability, cardiovascular coupling, time series analysis**

I. Introduction

Increasing evidence demonstrates that gender-related factors influence physiological mechanisms of the cardiovascular system and the cardiac autonomic regulation [1]–[3]. Up to now the assessment of gender-related differences has been focused on the calculation of the most widely applied heart rate variability (HRV) indices, leading to conflicting results and not univocal conclusions [1], [2]. Most studies tend to suggest that young women exhibit a shorter mean heart period and lower sympathetic activity [1]–[3]. Even less is known about gender-related differences in blood pressure variability, although women are usually characterized by lower blood pressure given their smaller overall heart size, often causing a lower orthostatic tolerance and reduced baroreflex control [3].

In this work, we aim to further explore gender-related differences in autonomic regulation on healthy young people exploiting information-theoretic measures able to assess the dynamical complexity of individual cardiovascular time series and the pairwise coupling between them [4], [5].

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II. Materials and Methods

The analyses were performed on HYPOL (Healthy Young POLes) database, collected at the Department of Cardiology-Intensive Therapy research laboratory, Poznan University of Medical Sciences, Poznan, Poland, and shared for the ESGCO Challenge 2024 [6]. Data consisted of beat-to-beat cardiovascular times series of young healthy subjects acquired during supine rest. From the original dataset, 276 subjects (147 women; age: 23.8 ± 2.6 years) were taken into account (data of 2 subjects were missing). For further information about the dataset and signal acquisition we refer the reader to [6]. 300-point electrocardiographic R-R interval (RR), systolic (SBP) and diastolic blood pressure (DBP) time series were considered, discarding the first 60 beats for each subject and time series. The RR time series did not include "technical artifacts" according to database description [6]. In this work, we computed the information-theoretic measure of entropy rate (ER), quantifying the rate of generation of new information in a random stationary process X and defined as [4]:

$$H_X = \lim_{m\to\infty} \frac{1}{m} H(X_{n:n+m}), \tag{1}$$

being n the present time, m the past lags and $H(\cdot)$ the entropy of X [4]. The ER reflects the complexity of the process, i.e. the unpredictability of its present state given the past, and thus quantifies the interactions of *order one* occurring internally in the process X. When taking into account two processes X and Y, it is possible to assess the pairwise interactions (i.e. of *order two*) between them using the measure of mutual information rate (MIR). The MIR quantifies the information shared by the two processes per unit of time and can be computed as:

$$I_{X;Y} = \lim_{m\to\infty} \frac{1}{m} H(X_{n:n+m}; Y_{n:n+m}), \tag{2}$$

where $H(\cdot;\cdot)$ is the joint entropy of the two processes. The measures can be also computed in the frequency domain starting from the power spectral density (PSD) matrix of the

stationary vector random process $[XY]$ [4]. The weighted covariance non-parametric approach was exploited to derive the PSD, using the biased estimator for the cross-correlation function and the Parzen window (bandwidth of 20 Hz) (refer to [4] for further details). Each measure was evaluated within the Low-Frequency (LF, [0.04-0.15] Hz) and High-Frequency (HF, [0.15-0.4] Hz) spectral bands. The ER measures were computed on RR, SBP and DBP time series to quantify their individual complexity, while the MIR was evaluated between each pair of time-series to assess the pairwise dynamical coupling, setting $m = 20$ according to [4]. Before estimating the measures, all time series were preprocessed applying a high-pass autoregressive filter (zero phase and cut-off frequency 0.0156 Hz). To assess gender-related differences of the ER and MIR measures, the unpaired parametric Student's t-test ($p < 0.05$) was applied to the distributions of the indices computed for males and females, respectively.

III. Results

Conventional time-domain analyses (i.e. average and standard deviation, not shown for brevity) evidenced statistically significant lower mean RR intervals and higher average systolic blood pressure values in females. Time-domain results of information-theoretic analyses (Fig. 1) indicate that females exhibit increased ER with regard to DBP only. Spectral decomposition allowed to highlight statistically significant lower ER values in females in LF band for RR and SBP time series (Fig. 1(a)). From MIR results (Fig. 1(b)) we infer that females exhibit a decreased dynamical coupling in LF band for all the pairwise interactions between the cardiovascular time series.

IV. Discussion and Conclusion

Our results evidence that females exhibit a lower complexity of RR and SBP dynamics within the sympathetic-related band, together with a reduced cardiovascular coupling. The findings explain the lower normalized LF power values reported in females (not shown for brevity), being the spectral ER related to band power (as detailed in [4]). Overall, these results support the findings in literature that evidence differences in autonomic function associated with blood pressure regulation with lower responsiveness and sympathetic support in young healthy females, eventually resulting in increased predisposition to orthostatic intolerance [3]. Gender-related differences in cardiovascular coupling even during resting supine condition were also evidenced in a previous work [3] using a different approach (Joint Symbolic Dynamics). Our results indicate that the lower sympathetic activity in females elicit a decreased cardiovascular coupling occurring mainly within the LF spectral band. Future activities should complete this work through a spectral analysis and MIR decomposition in its causal components [7].

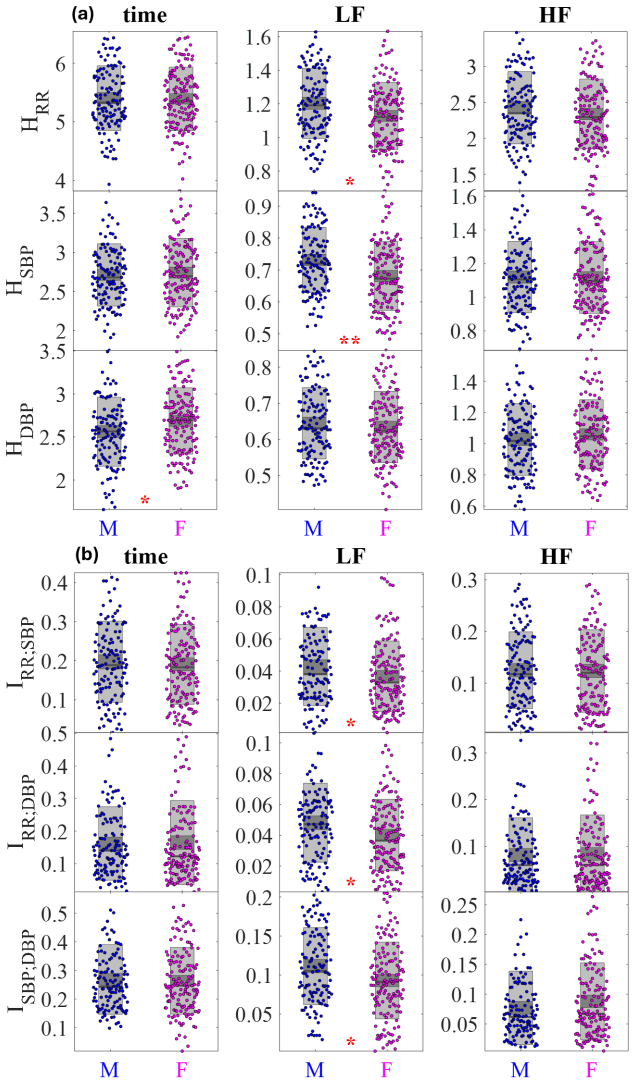

Fig. 1. Boxplot distributions and individual values of (a) ER and (b) MIR time-domain and spectral measures integrated in LF and HF bands. Statistical test: Student's t-test: *,$p < 0.05$;**,$p < 0.001$, males (M) vs females (F).

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