# Scaling behavior in the heart rate variability characteristics with age

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**Abstract**

In this work we study the characteristics of the heart rate variability (HRV) as a function of age and gender. The analyzed data include previous results reported in the literature. The data obtained in this work expand the range of age studied until now revealing new behaviors not reported before. We analyze some measurements in the time domain, in the frequency domain and nonlinear measurements. We report scaling behaviors and abrupt changes in some measurements. There is also a progressive decrease in the dimensionality of the dynamic system governing the HRV, with the increase in age that is interpreted in terms of autonomic regulation of cardiac activity.

## 1 Introduction

Heart rate variability (HRV) is the physiological variation in the duration of cardiac cycles [1,2]. With the development of electrocardiographic devices the term was related to the variation in the duration of the RR-intervals in an electrocardiographic record. The HRV is mainly controlled by the autonomic nervous system (ANS) through the interplay of sympathetic and parasympathetic neural activity mainly at the sinus node [3,4]. In general, the HRV is influenced by many several factors such as chemical, hormonal and neural modulations, circadian changes, exercise, emotions, posture and preload. The adaptation of the

heart rate to changing factors is carried out by the activity of different regulatory subsystems, i.e. activity of vasomotor and respiratory centers, of baroreflex and chemoreflex closed loop regulation, of cardiovascular reflexes mediated by vagal and sympathetic afferences, and of vascular and thermoregulation. The variety of regulatory subsystems results in a complex linear and nonlinear temporal behavior, which changes with age and pathologic conditions. Several studies demonstrated age-related and gender-related variation in long-term HRV characteristics. It was reported that autonomic activities diminish with age in both genders and that gender-related variation in parasympathetic regulation decreases after the age of 50 years [5-11].

HRV characteristics were proposed as predictors of the risk of premature mortality after myocardial infarction or development of congestive heart failure, diagnosis of autonomic dysfunction in diabetes, non-invasive estimation of the autonomic modulation of the cardiovascular system during stress, relaxation or the assessment of the effects of physical training on fitness level. All of these are the reasons why the interest in HRV is growing both in clinical and physiological studies [12-19].

Many mathematical methods to compute the HRV characteristics have been developed—they may be grouped into statistical, spectral, graphical, nonlinear, complexity, or information based[20-23].

In summary, there has been a huge effort from the world scientific and medical community to have reliable measurements of the HRV characteristics in normal and pathological conditions. Concerning the relationship of HRV with gender and age, very extensive and complete studies can be found in [2, 24] and references therein, which both together constitute the broadest study of the HRV relationship with age we know.

In this work *we expand the range of age studied in the literature and reveal new behaviors that had not been detected until now.* We include data from previous studies and show that our data are consistent with them. We also analyze differences by gender. Our study is limited to the study of some of the existing measurements, but the results show the need to reanalyze all the others, and a further analysis (with additional insights into the treatment of data) will be presented later.

This work is organized as follows: in the next section methodological details are explained. They are equal to those also used in [21,22] and comparable to the methodology used in [2, 24].

Section 3 shows the results first as a function of age and then distinguishing among genders. Dependences are rationalized adjusting power law behaviors.

Finally we summarize our conclusions in Section 4.

| | |
|---|---|
| I | Minimal nighttime frequency¿60/min |
| II | Nighttime pauses¡3 seg. |
| III | Ventricular extrasystoles ¡ 100/24h, without couplets, bursts or polymorphism. |
| IV | Supraventricular extrasystoles ¡ 100/24h, without bursts. |
| V | Absence of blocks or conduction disturbances. |

Table 1: Normality criteria for all Holters recorded in the present work.

## 2 Procedure

Holter recordings from healthy subjects were collected from volunteers after an exhaustive interview and clinical examination. Those individuals without clinical symptoms of disease, without medication and with electrocardiograms (ECG) within normal parameters according to the criteria summarized in Table 1 were included[25,26].

Holters were recorded for 24 h with digital three-channel DMS300 7 and DMS300 3A recorders, and Galix recorders, using 3M electrodes[27]. The automatically detected and classified electrocardiographic recording events were examined and corrected by two cardiologists, and the artifacts were removed as aforementioned.

We applied quality criteria established in [25,26] to the all time series used in the present work. Also stationarity was evaluated and surrogate analysis was performed as in [28-31].

Time series of a total of 195 healthy individuals were finally analyzed (13 time series were taken from [32], and 28 from [33]). They are from 0 to 74 years old and 50% of them are females.

In Results we also introduced data from [2,24] for comparison purposes. In total, data of about 500 healthy subject aged between 1 month and 99 years were evaluated.

## 3 Results

### 3.1 Linear analysis

The following linear indexes in the time domain were calculated: the RR interval mean value, $< RR >$, the standard deviation, $SD_{RR}$, the square root of the mean of the sum of the squares of differences between consecutive RR intervals , $rMSSD_{RR}$, and the percentage of the intervals that vary more than 50 ms from the previous interval, $pNN50$.

Figure 1 shows their dependence on age, including data from [2] and [24]. Data from different sources show a good agreement among them validating the general treatment of the measurements. Our data expand the experimental range of age revealing unknown tendencies. Indeed while $< RR >$ exhibits a monotonic behavior, $SD_{RR}$, $rMSSD_{RR}$ and $pNN50$ show an abrupt change at the age of 12 years not detected so far. We rationalized Figure 1 results through scaling laws as follows:

$$< RR >= (515 \pm 2)x^{(0.117 \pm 0.003)} \tag{1}$$

$$SD_{RR} = \left\{ \begin{array}{ll} (79.4 \pm 0.8)x^{(0.25 \pm 0.01)} & x < 12 \\ (295 \pm 12)x^{(-0.22 \pm 0.03)} & x > 12 \end{array} \right\} \tag{2}$$

$$rMSSD_{RR} = \left\{ \begin{array}{ll} (18,6 \pm 0.2)x^{(0.34 \pm 0.02)} & x < 12 \\ (166 \pm 11)x^{(-0.46 \pm 0.04)} & x > 12 \end{array} \right\} \tag{3}$$

$$pNN50 = \left\{ \begin{array}{ll} (0.037 \pm 0.001)x^{(0.78 \pm 0.07)} & x < 12 \\ (5 \pm 1)x^{(-1.1 \pm 0.1)} & x > 12 \end{array} \right\} \tag{4}$$

where $x$ is the age in years.

Though the power law adjustments for ages above 12 years are statistically worse than those for ages below 12 years, they are still better than or equal to other linear or quadratic adjustments performed on the same sets.

Gender differences are shown in Figure 2, and Table 2 summarizes the power law parameters in each case. For ages below 12 years there are no significant differences with gender, while for ages above 12 years, a slight but significant difference appears in $SD_{RR}$ and $pNN50$ (see Table 2)

### 3.2 Frequency domain measurements

Heart rate variability time series exhibit power law behavior in the frequency (1/beat) domain, which is manifested in the power spectrum behavior and expressed as

$$S(f) \alpha f^{\beta} \tag{5}$$

| Index | Male | | | Female | | |
|---|---|---|---|---|---|---|
| $< RR >$ | Eq. | $506(4)x^{0.125(5)}$ | | Eq. | $500(3)x^{0.115(4)}$ | |
| | N | 182 | | N | 213 | |
| | R | 0.94 | | R | 0.95 | |
| | p¡ | $10^{-4}$ | | p¡ | $10^{-4}$ | |
| $SD_{RR}$ | | below 12 | above 12 | | below 12 | above 12 |
| | Eq. | $77.6(8)x^{0.27(3)}$ | $398(4)x^{-0.28(4)}$ | Eq. | $77.6(8)x^{0.21(3)}$ | $229(2)x^{-0.17(4)}$ |
| | N | 57 | 123 | N | 50 | 148 |
| | R | 0.86 | $-0.55$ | R | 0.80 | $-0.36$ |
| | p¡ | $10^{-4}$ | $10^{-4}$ | p¡ | $10^{-4}$ | $10^{-4}$ |
| $rMSSD_{RR}$ | | below 12 | above 12 | | below 12 | above 12 |
| | Eq. | $19.5(8)x^{0.36(3)}$ | $200(20)x^{-0.54(7)}$ | Eq. | $18.2(8)x^{0.34(4)}$ | $160(20)x^{-0.45(6)}$ |
| | N | 58 | 125 | N | 55 | 143 |
| | R | 0.83 | $-0.57$ | R | 0.79 | $-0.51$ |
| | p¡ | $10^{-4}$ | $10^{-4}$ | p¡ | $10^{-4}$ | $10^{-4}$ |
| $pNN50$ | | below 12 | above 12 | | below 12 | above 12 |
| | Eq. | $0.038(2)x^{0.8(1)}$ | $12(2)x^{-1.4(2)}$ | Eq. | $0.037(2)x^{0.7(1)}$ | $1.7(1)x^{-0.8(1)}$ |
| | N | 58 | 124 | N | 53 | 133 |
| | R | 0.76 | $-0.63$ | R | 0.67 | $-0.43$ |
| | p¡ | $10^{-4}$ | $10^{-4}$ | p¡ | $10^{-4}$ | $10^{-4}$ |

Table 2: Power law adjustments by gender and age range (where $x$ is the age). The numbers parentheses indicate the error in the parameters, N is the number of data, R is the correlation coefficient and p is the t-Student parameter.

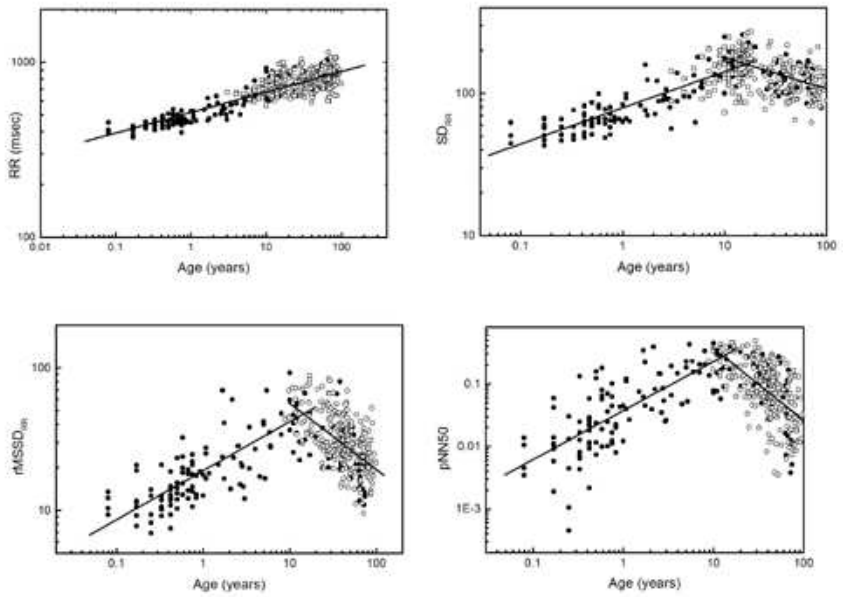


Figure 1: Age dependence of some statistical indexes. Filled circles are the data of this work, open squares are data from [2], and open circles are data from [24].

$\beta$ values were determined in this work by averaging the power spectra of successive time series segments of 4096 beats. An example is shown in Fig. 3. The procedure allows the elimination of high frequency fluctuations and is detailed in [26]. Other frequency domain measurements were defined such as the low frequency (LH) and high frequency (HF) indexes and their ratio (LF/HF), etc. They will be discussed in a further work in comparison with other short term measurements.

Figure 4 shows the dependence of $\beta$ on age. A nonmonotonic behavior is observed which was no reported so far: an increase of $\beta$ values appears at the interval extremes, where the action of each one of the subsystems of the ANS dominates (either sympathetic or parasympathetic tones). Also a minimum at the age of 1 year, is revealed which was not reported so far and deserves to be further explored.

### 3.3 Nonlinear analysis

Heart rate variability time series can be thought as a sequence of observations $s_n$ performed on a multidimensional dynamic system.

To unfold the multidimensional structure of the system by using a scalar sequence $s_n$ of data, the method of delays is employed in nonlinear sciences.

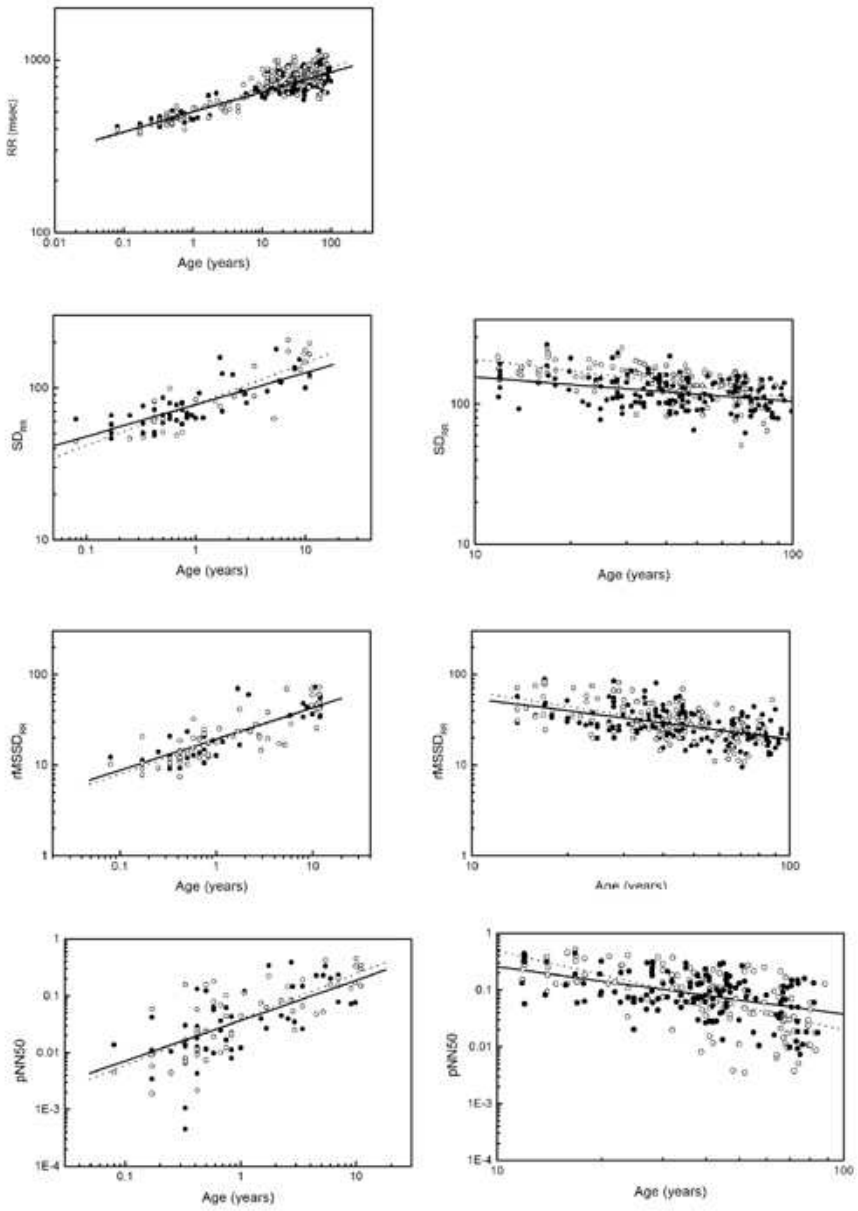


Figure 2: Gender effect on different statistical indexes. Filled circles are female subjects and open circles are male subjects. Panels on the left show the adjustments for ages below 12, while panels on the right show the adjustments for ages above 12. The adjustment parameters are shown in Table 2. Solid lines correspond to female subjects and broken lines correspond to male subjects.

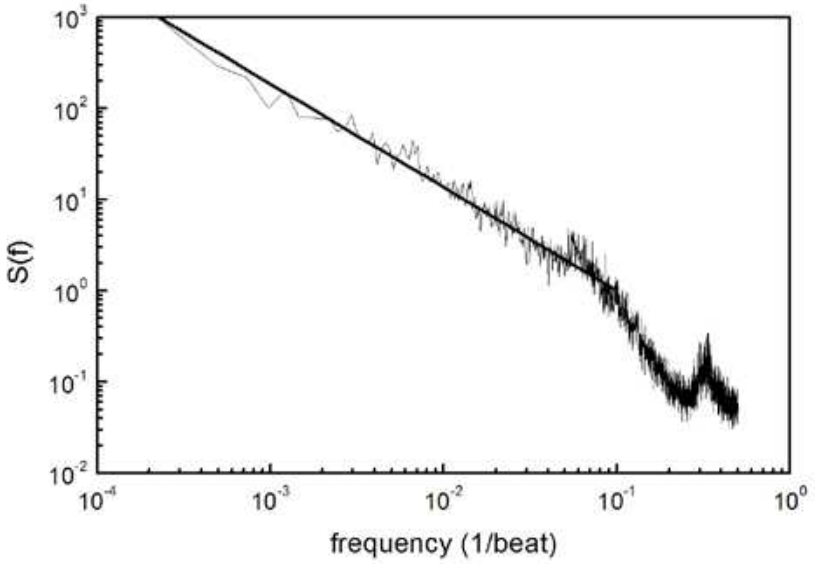


Figure 3: Averaged power spectrum of a healthy adult subject and linear adjustment at low frequencies to determine $\beta$. For details see [26]

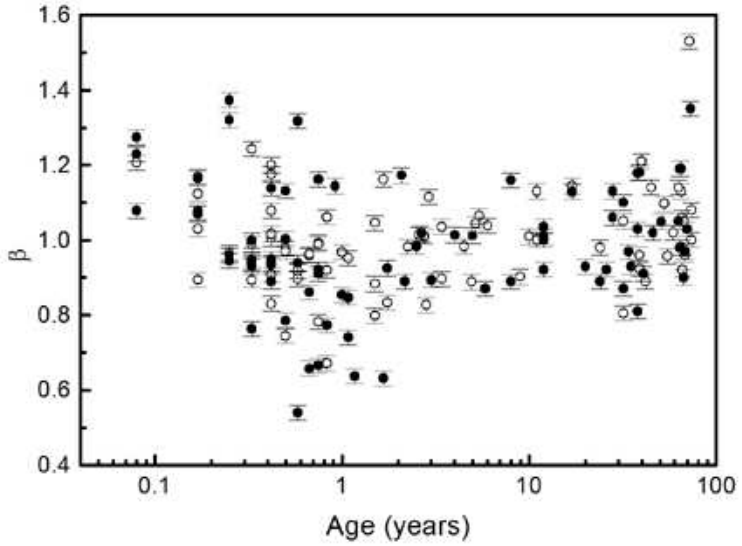


Figure 4: $\beta$ dependence on age and gender. Filled circles are female subjects and open circles are male subjects

Vectors in an embedding space are formed from time-delayed values of the scalar measurements $s_n = (s_{n-(m_0-1)\tau}, s_{n-(m_0-2)\tau}, \ldots, s_n)$ , where $m_0$ is the minimal embedding dimension and $\tau$ is the delay time. Both $m_0$ and $\tau$ provide fundamental information on the dynamic system;$m_0$ gives the dimension to completely unfold the trajectory of the system in the phase space.

The false nearest neighbor (FNN) method was proposed by Kennel et al. to determine $m_0$ [34]. The idea is very intuitive and is based on the fact that in the embedding dimension ($m_0$), the trajectories or the attractor reconstructed from a physical observable by the delayed coordinate method are a biunique image of the attractor in the original phase space. In particular, the topological characteristics of the attractor are preserved, despite the changes in the radii of curvature, the trajectories and the radius of the neighborhood of a point (according to Lyapunov exponents). Hence, the false nearest neighbor method consists of reconstructing the attractor in progressively greater$m < m_0$ dimensions and determining the number of average neighbor points (within a neighborhood of radius $\varepsilon$ ) of each of the attractor points. As the topologies of the original attractor projections are not necessarily preserved in the reconstructed attractor, a point belonging to a neighborhood for a given m value may belong to another neighborhood for a greater $m$ value. We will then say that in our neighborhood that point was a false nearest neighbor.

The method consists of calculating the false nearest neighbor fraction for progressively larger values of $m$ . When $m = m_0$ , the false nearest neighbor fraction should stabilize and ideally take a zero value. In practice, we determined $m_0$ as the value of $m$ where the false nearest neighbor fraction curve stabilizes, i.e, that the absolute difference between two successive values is less than0.0005.

Eventually, the result also depends on both the length and the delay time $\tau$ of the time series, and an adequate comparison of the results will require a careful evaluation of the algorithm and the standardization of the procedures used. In this study we used the nearest neighbor algorithm provided by the TISEAN software package [35,36]. We chose a value of $\tau = 1$ for all the time series. This value, as well the algorithm performance as a function of the length of the time series, has been tested previously in our work.

The $FNNF10$ index is just the nearest neighbor fraction for $m = 10$ (regardless of the $m_0$ value). This magnitude may be taken as a measure of the error in the reconstruction of the attractor for that value of $m$.

Figure 5 shows the dependence of $m_0$ on age and gender.

Figure 6 shows the dependence of FNNF10 on age for different genders. The results were rationalized

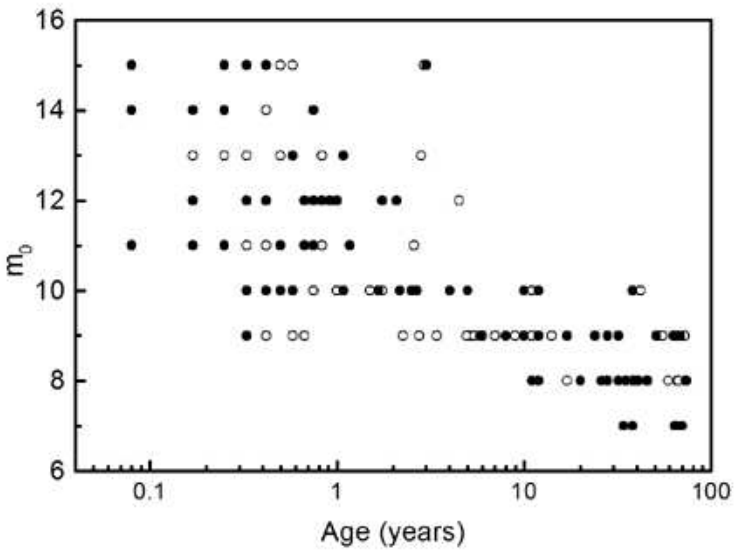


Figure 5: $m_0$ dependence on age and gender. Filled circles are female subjects and open circles are male subjects

adjusting scaling equations as follows:

$$FNNF10 = 0.065(3)x^{-0,75(5)} \tag{6}$$

$$FNNF10 = 0.072(4)x^{-0,79(5)} \tag{7}$$

where x is the age and Eq (6) is valid for males while Eq (7) is valid for females.

## 4 Discussion and Conclusions

Data analyzed in the present work are of different sources and correspond to about 500 healthy subjects covering the most large range of ages analyzed so far. In the present work 195 records were acquired. There are many other studies based on age and gender in the literature. Although the results reported by them are consistent with ours, a direct comparison was not possible because of the way in which the data were reported. The age of the individuals should be considered as a continuous variable to detect the functional dependences as reported in this work.

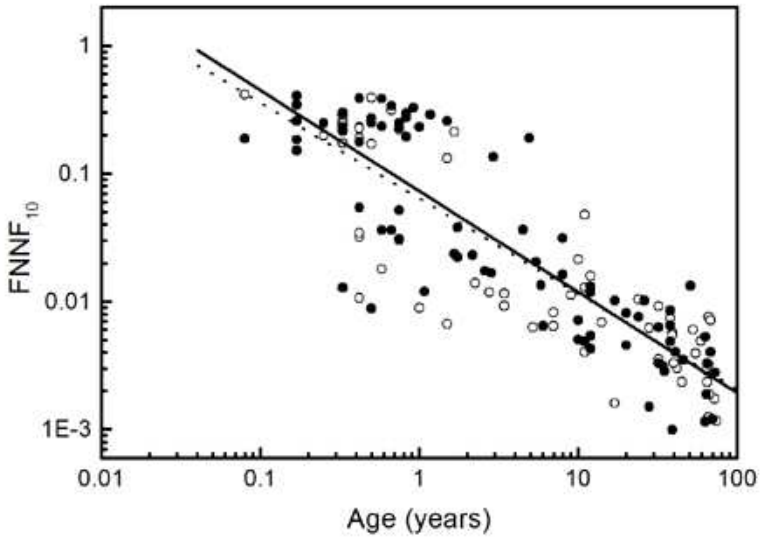


Figure 6: $FNNF_{10}$ dependence on age and gender. Filled circles are female subjects and open circles are male subjects. The broken line corresponds to Eq. (6) and the solid line to Eq. (7).

The main conclusions are:

$< RR >$follow a scaling relationship with age that is independent of gender.

Statistical measures such as $SD_{RR}$, $r - MRSSD_{RR}$ and $pNN50$ show an abrupt change at the age of 12 years. We assume the same cutoff (independent of gender) in all cases for simplicity, but this ansatz should be further studied. Below 12 years, the results are independent of gender, while above 12 years there seems to be a slight dependence on gender.

Other statistical measures also deserve to be explored.

Two previously developed non linear measurements, $m_0$ and $FNNF10$, were also studied as a function of age and gender. $m_0$ is the minimum number of topological dimensions to unfold the dynamical system governing the HRV. It is highly variable among individuals but it is always higher than 9 for ages below 10 years and always lower than 10 for ages up to 10. $FNNF10$ is the nearest neighbor fraction for $m = 10$ (regardless of the $m_0$ value). This magnitude diminishes with age also following a scaling behavior that is independent of gender. The decrease of $FNNF10$ is consistent with the fact that $m_0$ takes values that for children are higher than those for adults. One could relate the behavior of the dynamic system to the changes in the autonomic modulation of HRV.

The autonomic activity diminishes with age in both genders, and the dynamic system evolves in a topological space of the decreasing dimension, i.e, with a progressively lower number of dynamic variables influencing the HRV.

These changes would also be reflected in the dependence of $\beta$ on age, but further studies are necessary to reveal them and they will be presented later.

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