

Aging of ECG Characteristics over a Five Year Period

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Abstract

The aim of this work was to find evidence of aging of ECG indicators in a population of young adults (52 subjects of age 19 ± 0.6 in 2002). For this purpose, an application which analyzes ECG signals was designed and implemented. The data consist in four different series for each subject of the studied population. Two ECG signals of 5 minute duration (one at rest and one after a mild effort) were taken in 2002 and the exact same procedure was repeated for each subject five years later in 2007.

All these electrocardiographic signals were examined by computational techniques in order to extract the RR and QT intervals and the energy content of the T-wave. Next, we have compared all the data using first return maps and measured the data dispersion by evaluating the covariance ellipses. Relations between each of the four data series were studied. The analysis also included the gender and the categorical aspect "practicing sport".

1. Introduction

The process of aging affects the cardiovascular system and results in alterations in the cardiovascular physiology and heart performance. Aging and illness have been related to a decreasing irregularity in the heartbeat [1] and a loss in complexity of the cardiovascular dynamics [2]. Several studies have been done in order to compare heart variability of subjects of different ages. Many of them concerning either elderly subjects or sample groups of distant ages [3–5].

ECG is a noninvasive method which registers the electrical activity of the heart over a period of time. Its analysis provides information about abnormalities of the cardiac activity and the regulation of the autonomic nervous system. Effects of aging have been associated to changes in some characteristics of the ECG waves, mainly decreased variability of the RR interval [6] and increased dispersion of the QT interval in elderly healthy subjects [4]. In ad-

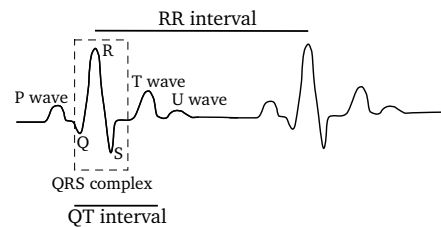


Figure 1. Main features of an ECG

dition, both QT and RR intervals' fluctuations are linked to the development of malignant arrhythmias [7] and used to diagnose several cardiac diseases. Abnormalities in the T-wave amplitude or morphology can also be associated to cardiac disorders.

First return maps are a non-linear dynamics tool which allow to understand relationship between consecutive points of a time series. The n th data is plotted on the x -axis versus the $n+1$ th which is plotted on the y -axis. They have been used to characterize the RR variability (HRV) and QT variability and they have been related to the Pearson coefficient, which has been proved to contain valuable clinical information [8]. In addition, they have also been pointed out as a potential tool for the detection of the T-wave alternans (TWA) [9]. Therefore, first return maps are a tool of choice in order to observe effects of aging in the cardiovascular dynamics of young adults. This study has focused on the RR interval; QT interval lengths and changes in the energy content of the T-wave.

2. Methods

2.1. Data acquisition

Two series of 5 minutes ECG signals were recorded at a sampling rate of 10 kHz in 2002. The first series at rest and the second one after a mild effort consisting of twenty knee flexions in standing position. Five years later, the same subjects were contacted again and the same examination was repeated following the exact same process. Two

new series of ECG signals were registered, one at rest and another one after the mild effort. In addition, every subject was asked to answer a few yes or no questions about gender, sport practice, smoking habits and medical condition related to cardiac diseases.

2.2. Data analysis

The data analysis was done using the commercial mathematical software *Matlab* [MATLAB Release R2012a, The MathWorks Inc., Natick, Massachusetts, United States] in several stages:

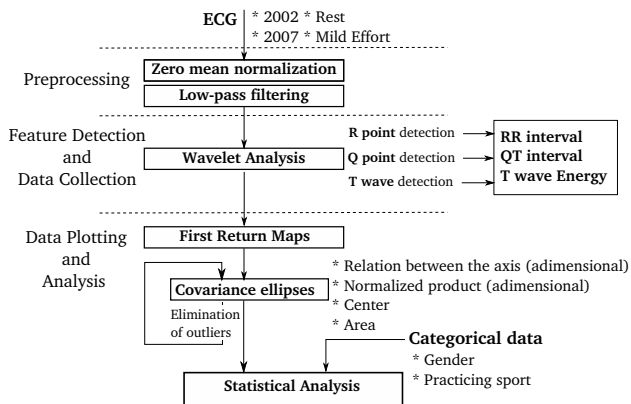


Figure 2. Data analysis procedure.

Preprocessing of the signal

First, the ECG signals were normalized to zero mean and some low-pass filtering was applied in order to smooth the signal.

Feature detection

The ECG feature extraction was done using wavelet analysis. Paul wavelet of order 4 was chosen because of its good time localization capability. R peaks were clearly identified in the low scales (4–20) corresponding to time between 22 and 111 ms while the T-wave peaks were better observed in the medium scales (43–79) corresponding to time between 240 and 441 ms. The T-wave limiting points and the beginning of the Q deflection were also extracted from the ECG. Finally, from the R, Q and T-end vectors, the intervals RR and QT were computed. The energy of the T-wave was calculated using the Euclidean norm of the wavelet coefficients taken from the beginning to the end point of the T-wave. Noisy data and subjects with known cardiac diseases were removed from the study leaving a final sample of 45 subjects (17 men - 28 women). Therefore, for each subject and each characteristic (RR intervals, QT intervals, T- energy) there were four data series: effort / basal (in the year 2002), effort / basal (in the year 2007).

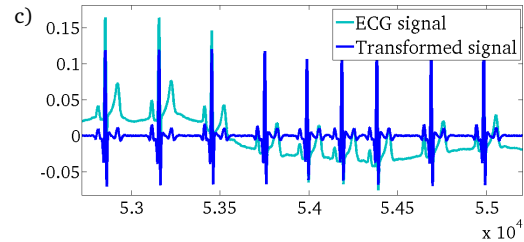
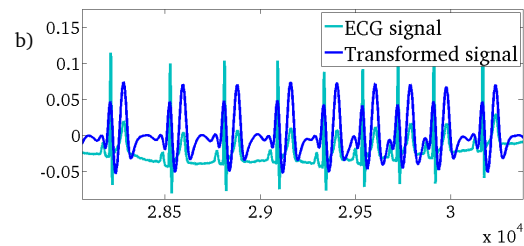
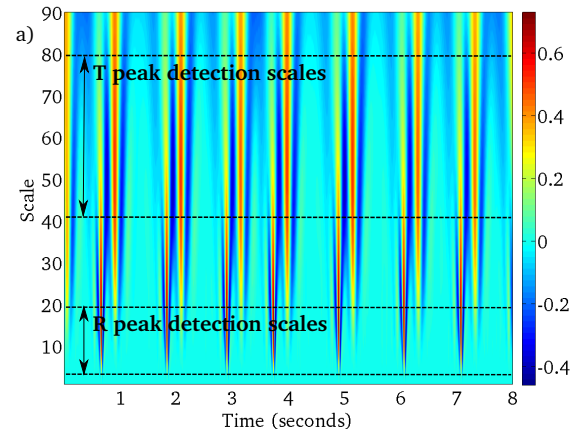


Figure 3. a) Paul wavelet coefficients, b) Example of filtered ECG for medium scales (T peak detection), c) Example of filtered ECG for low scales (R peak detection).

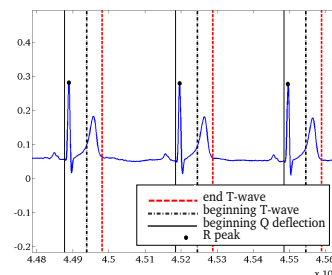


Figure 4. ECG - feature detection

First return maps and covariance ellipses

For every subject 12 first return maps were obtained and plotted in pairs for years 2002 and 2007. Every point cloud was approximated by its covariance ellipse¹. Points whose projections on the semi-axes of the ellipse were greater

¹See Appendix

than 2.5 times the corresponding semi-axis' length were considered outliers and eliminated. After the outliers removal, the ellipses were recalculated and plotted again as shown in Fig. 5. Covariance ellipses were quantified us-

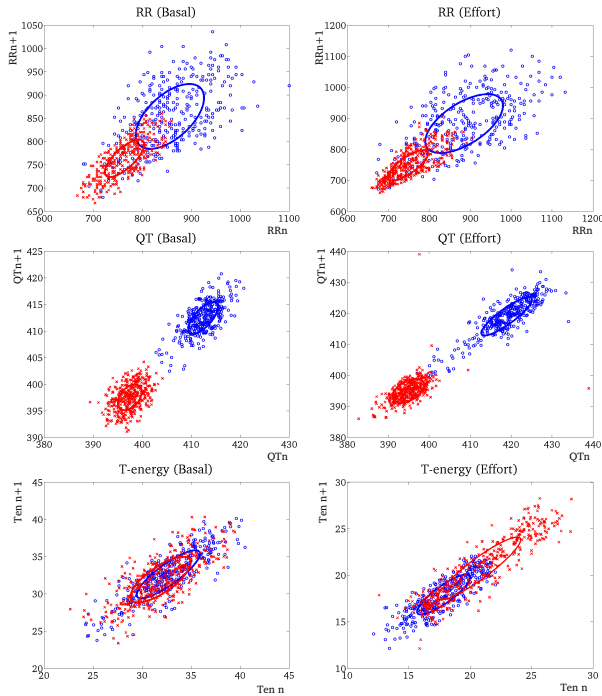


Figure 5. 12 point clouds corresponding to one subject. In descending order: First return maps of RR interval, QT interval and T-wave energy and the corresponding covariance ellipses at rest (left) and after a mild effort (right). 'o' (blue symbols) correspond to 2002 and 'x' (red symbols) to 2007.

ing several indicators, i.e., the ratio between the semi-axes of the ellipse a/b , the product of the semi-axes ab (proportional to the area) and the normalized product of the semi-axes $norm(ab) = \frac{ab}{x^2+y^2}$ where (x, y) are the coordinates of the center of the covariance ellipse. The area and shape of the ellipse are related to the variability of the data series. Larger ellipses correspond to larger differences between consecutive points and therefore more variability. Normalized product allows for a correction on the area with respect to the ellipse center. Information about the shape is contained in the ratio of the semi-axes. More circular ellipses ($a/b \simeq 1$) are related to a great variability between consecutive intervals while elongated ellipses along the first bisectrix ($a/b \gg 1$) correspond to great variability but smooth change between consecutive beats. Elongated ellipses on the other direction ($a/b \ll 1$) show more irregular fluctuations from beat to beat.

Statistical analysis

Relations between the different data series (effort/rest,

2002/2007) were studied for every characteristic (RR intervals, QT intervals, T- energy) and all the indicators (a/b , ab , $norm(ab)$). The analysis included the gender and the regular practice of sport. Lilliefors test was used to check normality. Due to non normality of the data non parametric statistics were used. There, we have used Kruskal-Wallis and Wilcoxon signed tests. Wilcoxon sign test was chosen because it is more robust to non-symmetric data. A p -value with $p < 0.05$ was considered statistically significant.

3. Results and conclusions

The studied population of young adults showed a significant reduction of the area of the RR ellipse after a period of 5 years (between the age of 19 to 24). This reduction was observed for both indicators, the product and normalized product of the semi-axes. Table 1 summarizes the differ-

Table 1. p -values for the comparison of the normalized product $norm(ab)$ between 2002 and 2007 for different groups.

$norm(ab)$		RR	QT	T-energy
	Basal	0.0066	NS	NS
	Effort	$8.24 \cdot 10^{-04}$	NS	0.0161
Basal	Men	NS	NS	NS
	Women	0.0037	NS	NS
Effort	Men	NS	NS	0.049
	Women	$9.12 \cdot 10^{-4}$	NS	NS
Basal	Sport	NS	NS	NS
	No-Sport	0.0026	NS	NS
Effort	Sport	NS	NS	0.0041
	No-Sport	0.0026	NS	NS

NS=No Significance

ences found in $norm(ab)$ between 2002 and 2007 for several groups. The area reduction for the RR interval can be observed in Fig.6. The normalized product of ab in 2002 is plotted in the x -axis and the normalized product of ab in 2007 in the y -axis. Points below the first bisectrix present a reduction of this indicator from 2002 to 2007.

An area reduction was not observed while analyzing the corresponding QT intervals. Significant differences in the normalized product between 2002 and 2007 were found for the T wave energy content of the effort signal in men and people who practiced sport. However, these differences are related to an increase and they cannot be directly associated to the process of aging.

The study with more groups (men-sport, men-no-sport, women-sport, women-no-sport) showed that women who did not practice sport is the group that suffered the most significant differences for both ab ($p = 0.0074$) and $norm(ab)$ ($p = 9.76 \cdot 10^{-4}$) in the RR effort signal. This

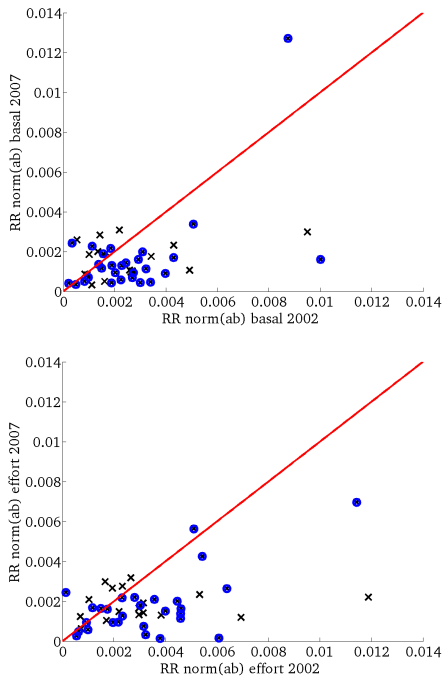


Figure 6. $norm(ab)$ 2002 vs $norm(ab)$ 2007 for the RR interval at rest (upper graph) and after mild effort (lower graph). 'Women' are indicated with 'o' (blue symbols) and 'Men' are indicated with 'x' (black symbols).

group also showed significant differences for the ratio of the semi-axes a/b of the basal signal of the RR interval ($p = 0.0352$).

This study shows that the process of aging affects the ECG from early stages of adulthood. The decrease of the area of the ellipses for the RR interval can be related to a decrease of the heart rate variability, already known for older stages. Women and people who do not regularly practice sport are specially affected by aging and this loss of variability.

Acknowledgments

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References

- [1] Goldberger AL. Is the normal heartbeat chaotic or homeostatic?. *News Physiol Sci*. 1991;6:87-91
- [2] Lipsitz LA, Goldberger AL. Loss of 'complexity' and aging. Potential applications of fractals and chaos theory to senescence. *JAMA*. 1992;267(13):1806-9.
- [3] Kaplan DT, Furman MI, Pincus SM, Ryan SM, Lipsitz LA,

and Goldberger AL. Aging and the complexity of cardiovascular dynamics. *Biophys J*. 1991;59(4): 945-9.

- [4] Ho-Ming Su, Heng-Chia Chiu, Tsung-Hsien Lin, Wen-Chol Voon, Hong-Wen Liu and Wen-Ter Lai. Longitudinal study of the aging trends in QT interval and dispersion in healthy elderly subjects. *Age and Aging* 2006;5(6):636-8
- [5] Reardon M, Malik M. Changes in heart rate variability with age. *Pacing Clin Electrophysiol*. 1996;19:1863-6.
- [6] Zhang J. Effect of age and sex on heart rate variability in healthy subjects. *J Manipulative Physiol Ther*. 2007;30(5):374-9.
- [7] Nahshoni E, Strasberg B, Adler E, Imbar S, Sulkes J, Weizman A. Complexity of the dynamic QT variability and RR variability in patients with acute anterior wall myocardial infarction: a novel technique using a non-linear method. *J Electrocardiol*. 2004;37(3):173-9.
- [8] Cheng-Deng Kuo, Gau-Yang Chen, Yia-Yi Wang, Ming-Jung Hung, Jen-Lin Yang. Characterization and quantification of the return map of RR intervals by Pearson coefficient in patients with acute myocardial infarction. *Autonomic Neuroscience* 2003;105(2):145-152.
- [9] Li fei, Zhao jie, Jia hui-lin, Zhang chun-yun, Zhu xiao-lei. Poincare Mapping: A Potential Method for Detection of T-wave Alternans. *Procedia Environmental Sciences* 2011;8:575-581.

Appendix

The covariance ellipse is obtained from the covariance matrix given by

$$M = \begin{pmatrix} var(RR_n) & cov(RR_n, RR_{n+1}) \\ cov(RR_n, RR_{n+1}) & var(RR_{n+1}) \end{pmatrix}$$

and is tightly related to the Pearson coefficient defined as

$$\rho = \frac{cov(RR_n, RR_{n+1})}{\sqrt{[var(RR_n)][var(RR_{n+1})]}}$$

Since $var(RR_n) \cong var(RR_{n+1})$, the covariance matrix can be written in terms of two values $u = var(RR_n)$ and $v = cov(RR_n, RR_{n+1})$, thus

$$M_{cov} = \begin{pmatrix} u & v \\ v & u \end{pmatrix}$$

with eigenvalues $u + v$, $u - v$ and corresponding eigenvectors $(1, 1)$ and $(1, -1)$. Eigenvectors point the direction of the semi-axes of the ellipse and the square root of its eigenvalues are their respective length.

$$a = \sqrt{u + v} \quad b = \sqrt{u - v}$$

The center of the ellipse has coordinates $(\overline{RR_n}, \overline{RR_{n+1}})$ were $\overline{RR_n} \simeq \overline{RR_{n+1}}$.

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