STUDY OF DIGITAL BLOOD PRESSURE AND LASER DOPPLER FLOWMETRY SIGNALS THROUGH A MULTISCALE ANALYSIS

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ABSTRACT

Multiscale entropy (MSE) analysis allows quantifying the complexity of time series over multiple time scales. MSE can be useful to identify impaired cardiovascular control. Therefore, to better understand the regulatory mechanisms of the peripheral cardiovascular system, we have processed digital blood pressure (BP) and laser Doppler flowmetry (LDF) signals from finger and forearm with MSE. BP and LDF signals have been recorded simultaneously on 6 healthy subjects before and after a vasodilator administration (glycerin trinitrate, GTN). Our results show that BP and LDF signals do not have a constant complexity over scales. Moreover, a minimum, which may reflect the cardiac activity, was identified on MSE profiles. For BP signals GTN induces changes in the complexity. We also note that, after GTN administration, the complexity of LDF signals from forearm is increased for the largest scales studied herein while no changes are observed for the one of LDF signals from finger.

Index Terms— Multiscale analysis, digital blood pressure, laser Doppler flowmetry, peripheral cardiovascular system, glycerin trinitrate

1. INTRODUCTION

Physiological signals are complex and involve regulation processes which operate over multiple time scales. These control mechanisms can be studied by quantifying the signals "complexity" [1, 2].

The multiscale entropy (MSE) analysis allows the evaluation of the complexity of time series over multiple time scales [3, 4]. Several works have shown that MSE can be useful to identify abnormalities in cardiovascular control [4, 5]. Numerous MSE studies have analyzed heart rate variability signals (HRV) issued from the central cardiovascular system (CVS) [4, 5, 6, 7]. They have shown, in particular, that age and congestive heart failure induce a loss of complexity in HRV signals [6, 7].

By contrast, only few studies have considered signals issued from the peripheral CVS [8, 9]. From our knowledge, only digital blood pressure variability (i.e. systolic and diastolic blood pressures) and laser Doppler flowmetry (LDF) signals, which reflect the blood perfusion [10, 11], have been computed separately with MSE [5, 8, 9, 12]. We herein propose to process - with MSE - digital blood pressure (BP) and LDF signals recorded simultaneously. LDF signals have been acquired on two sites: the finger and the forearm. Finger and forearm do not present the same microvasculature structure. Therefore, control mechanisms involved for finger could be different from the ones of the forearm. To evaluate the peripheral CVS, we also propose to observe the possible impact of a chemical perturbation. For this purpose, a vasodilator (glycerin trinitrate, GTN) which reduces peripheral arterial resistances was administrated [13].

2. MATERIALS AND METHODS

2.1. Measurement procedure

For this study, BP and LDF signals were recorded simultaneously on six healthy subjects (30 $\pm$ 12 years old; 5 men), without known disease. All subjects gave their informed and written consent to participate to the study which was approved by the local ethic committee of our institution. For the acquisition, the subjects were in supine position. A BMEYE monitor (Nexfin, model 1, Amsterdam, sampling rate equal to 200 Hz) and a laser Doppler flowmeter (Periflux PF5000, Perimed, Sweden - 780 nm laser diode) were used for the acquisition of digital BP (left middle finger) and LDF signals respectively. Two LDF probes (PF408, Perimed, Stockholm, Sweden) were positioned on the finger (palm side) and on the

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forearm (ventral face) of the subjects. BP was assessed in mmHg and skin blood flow in arbitrary units (a.u.). Moreover, BP and LDF signals were recorded on a computer via an analog-to-digital converter (Biopac System) with a sampling frequency of 20 Hz for at least 30 min before GTN administration and 30 min after GTN administration (GTN, sublingual spray called Natispray, 2 doses of 0.15 mg, Teofarma, Italy). BP and LDF data for one subject are shown in Figure 1. The electrocardiogram (ECG) was also recorded, simultaneously to the acquisition of BP and LDF signals, with a physioflow device (PF-05 lab1, Manatec, France). Heart rate variability (HRV) signals were then computed from ECG and the average heart rate was estimated before and after GTN administration.

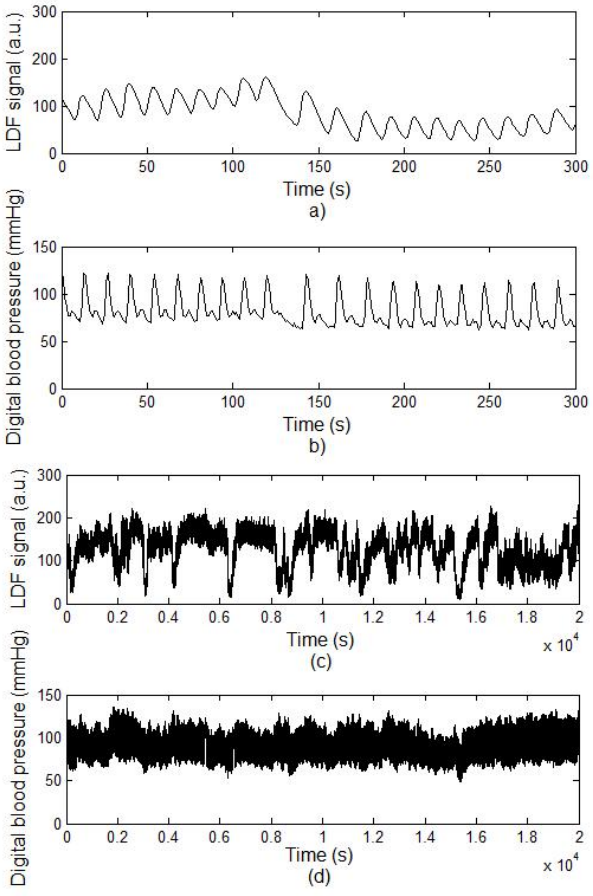

Fig. 1. a) LDF signal recorded on the forearm of one subject. b) digital blood pressure recorded on the same subject. c) same LDF signal as a) but represented on a longer time axis. d) same digital blood pressure as b) but represented on a longer time axis.

2.2. Multiscale entropy

In 1991, Pincus has introduced the approximate entropy (ApEn) to quantify the regularity of time series (i.e. presence of similar patterns in the time series) [14]. ApEn algorithms have largely been used to analyze physiological time series. However, ApEn requires quite long recording and lacks consistency. Therefore, Costa *et al.* have proposed the multiscale entropy (MSE) concept which allows analyses of short and noisy physiological time series [3, 4]. MSE consists in obtaining the entropy values, which are a measure of uncertainty, through several scales. For this purpose, given a time series $\{x_1, ..., x_i, ..., x_N\}$ of length N, a consecutive coarse-grained time series $y^{(\tau)}$ is constructed:

$$y_j^{(\tau)} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i \qquad (1)$$

where τ represents the scale factor and $1 \leq j \leq N/\tau$. The sample entropy (SampEn) of each coarse-grained is then computed. $SampEn(m, r, N)$ is the negative natural logarithm of the conditional probability that a dataset of length N, having repeated itself within a tolerance r for m points, will also repeated itself for $m + 1$ points, without allowing self-matches:

$$SampEn(m, r, N) = -\ln \frac{A^m(r)}{B^m(r)} \qquad (2)$$

where $A^m(r)$ is the probability that two sequences will match for $m + 1$ points and $B^m(r)$ is the probability that two sequences will match for m points. The more regular and predictable a time series, the lower the value of SampEn. The more random a time series, the higher the value of SampEn. To allow comparisons with previous studies [8, 9, 12], MSE algorithm was implemented with $m = 2$ and $r = 0.15 \times SD$, where SD is the standard deviation of the original time series.

Our BP and LDF data have been normalized before the application of MSE (substraction of the mean and division by the standard deviation). Moreover, our BP and LDF recordings having a length of 36 000 samples, they were processed with a scale factor τ ranging from 1 to 36 in order that the shortest coarse-grained time series contain 1000 points [15].

2.3. Data analysis

Statistical tests were computed with the TANAGRA software [16]. The Wilcoxon signed-rank test was used to compare BP data with LDF data recorded on finger and forearm, before and after GTN administration. Tests were considered as significant when p-value was inferior to 0.05.

3. RESULTS

Our results show that MSE profiles for both BP and LDF signals are nonmonotonic (see Figures 2 and 3 respectively).

SampEn values increase to reach a maximum, decrease to reach a local minimum and then increase again.

Before GTN administration, no significant differences between SampEn values of LDF signals recorded on the finger and the ones of LDF signals from the forearm are observed ($p > 0.05$ on all scales).

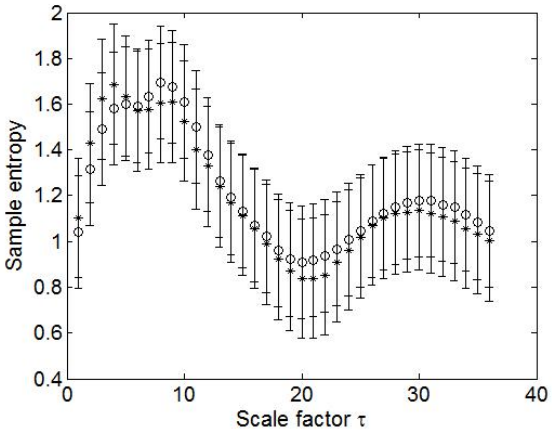

Fig. 2. Average SampEn of 6 digital blood pressure signals before GTN administration (circle) and after GTN administration (star).The sampling period for these signals is T = 0.052 s, which gives, for scale factors going from τ = 1 to τ = 36, time scales ranging from τT = 0.05 s to τT = 1.8 s. Vertical bars represent the standard deviation.

On MSE profiles of BP signals we can identify a local minimum (see Figure 2). This local minimum SampEn value is reached for a scale factor τ equal to 20 (scale factor corresponding to the minimum SampEn value observed on the average MSE profile of the 6 subjects). This distinctive scale is also present on MSE profiles of LDF signals from finger and forearm: τ = 18 and τ = 19 respectively (see Figure 3). However, the local minimum is more rounded. After GTN administration, SampEn values for BP signals are significantly increased on scale factors τ from 2 to 4 and decreased on scales 8, 11 and 19 to 23 (see Figure 2). Moreover, GTN administration significantly increased SampEn values for LDF signals recorded on the forearm on scale factors τ from 12 to 36 ($p < 0.05$)(see Figure 3b). However, GTN does not change significantly SampEn values for LDF signals from finger on all scales ($p > 0.05$)(see Figure 3a). We also note that SampEn values for LDF signals from forearm are higher than the ones of LDF signals from finger on scales from 15 to 36 after GTN admnistration.

4. DISCUSSION

In this study we processed BP and LDF signals issued from the peripheral CVS. LDF signals have been recorded on different sites: the finger and the forearm. Moreover, to better

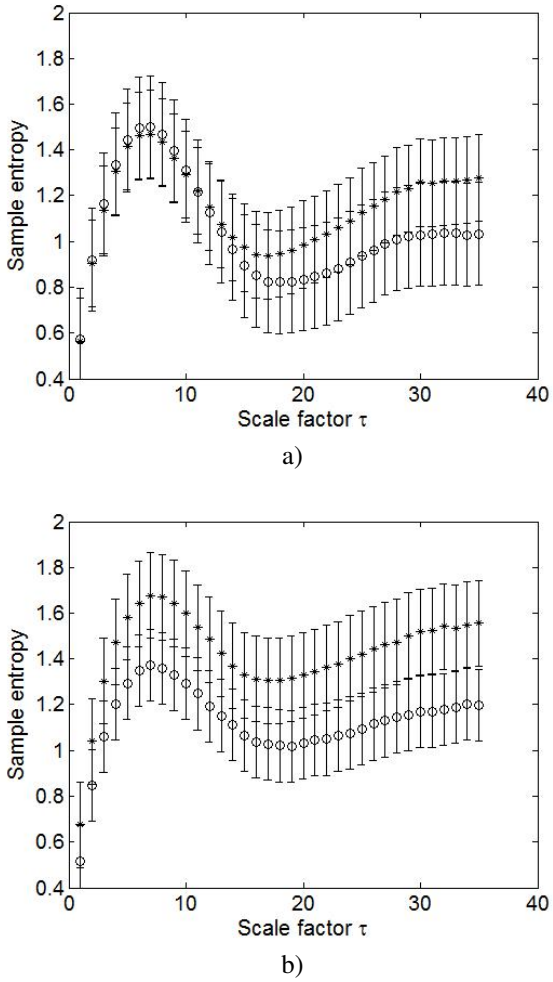

Fig. 3. a) Average SampEn of 6 LDF signals recorded on finger before GTN administration (circle) and after GTN administration (star). b) Average SampEn of 6 LDF signals recorded on forearm before GTN administration (circle) and after GTN administration (star).The sampling period for these signals is T = 0.05 s, which gives, for scale factors going from τ = 1 to τ = 36, time scales ranging from τT = 0.05 s to τT = 1.8 s. Vertical bars represent the standard deviation.

understand the underlying regulatory mechanisms of the peripheral CVS we have perturbed the CVS with a vasodilator, GTN. Our results show that MSE profiles of BP and LDF are nonmonotonic. SampEn values increase to reach a maximum. Therefore, the processes acting around the time scale corresponding to this maximum SampEn value have the highest irregularity. Then, SampEn values decrease to reach a local minimum. The processes acting around the time scale corresponding to this local minimum SampEn value have the lowest irregularity. The behavior of the MSE of continuous BP signals is different for the one of blood BP variability shown in previous studies [5, 12]. In supine position, SampEn values

of systolic and diastolic blood pressures increase with scales which is different from the nonmonotonic MSE evolution that we observe in our study. If we analyze systolic or diastolic blood pressure we remove the periodicity of the signal due to the cardiac activity and therefore the local minimum SampEn value dominated by the heart rate is not present on MSE profiles. In a previous study, Humeau *et al.* [9] have already suggested that the distinctive scale observed on MSE profiles of LDF signals could be dominated by the cardiac activity. If we multiply these scale factors by the sampling period $T = 0.05$ s, we obtain time periods equal to 0.9 s and 0.95 s which is close to the cardiac period. Moreover, if we compare this distinctive scale factor τ with the average heart rate (HR) estimated from HRV signals recorded during 30 min before GTN administration, for each subject, we find similar values (see Tables 1 and 2). The small difference observed could rely on the sampling period of BP and LDF signals which is higher than the one of ECG (0.05 s *vs* 0.004 s). When we compare, for each subject, the scale factor τ which corresponds to the average minimum SampEn value obtained from MSE profiles of LDF signals from finger and forearm, we find values rather similar although they are less close than the ones of BP and HR (see Tables 1 and 2). The local minimum present on MSE profiles of LDF signals is more rounded than the one present on MSE profile of BP. Therefore, the identification of the distinctive scale may be less accurate.

After GTN administration, the heart rate of some subjects has increased. For these subjects, we observed a shift of the MSE minimum value toward the left (i.e. toward smaller scale factors τ which correspond to higher frequencies) on both MSE profiles of BP and LDF signals. Therefore, this result may confirm the hypothesis that the distinctive scale corresponding to the local minimum SampEn value is dominated by the cardiac activity.

As regard the complexity, before GTN administration, SampEn values of LDF signals from the finger are not significantly different from the ones of LDF signals from the forearm on all scale factors although finger and forearm have different microvascular structures. However, after GTN administration, the complexity of LDF signals from forearm is increased for scales larger than 12 while no significant changes are observed for LDF signals from finger on all scales. Therefore, when CVS is perturbed by GTN, the processes which regulate the cutaneous blood perfusion in forearm may become less predictable and less regular on scale larger than 12. For BP signals, according to our results, after GTN administration, the irregularity of processes acting around small scales (2, 3 and 4) may be increased while the one of processes acting around larger scales (8, 11 and 19 to 23) may be reduced.

Table 1. Comparison between scale factor τ which corresponds to the minimum SampEn value on MSE profiles of BP signals and the average heart rate (HR) estimated from HRV signals recorded during 30 min before GTN.

Subjects	τ which corresponds to the local minimum SampEn value on MSE profiles of BP signals	Average HR (in second) estimated from HRV signals recorded during 30 min before GTN
subject 1	24 = 1.20 s	1.15
subject 2	12 = 0.60 s	0.62
subject 3	19 = 0.95 s	0.95
subject 4	19 = 0.95 s	0.98
subject 5	19 = 0.95 s	0.99
subject 6	15 = 0.75 s	0.74

Table 2. τ which corresponds to the minimum SampEn value on MSE profiles of LDF signals from finger and forearm (average τ from finger and forearm)

Subjects	τ which corresponds to the local minimum SampEn value on MSE profiles of LDF signals from finger and forearm (average)
subject 1	20 = 1.0 s
subject 2	12 = 0.60 s
subject 3	17 = 0.85 s
subject 4	19 = 0.95 s
subject 5	17 = 0.85 s
subject 6	14 = 0.70 s

5. CONCLUSION

Our analysis shows that both BP and LDF signals have a nonmonotonic MSE evolution. Moreover, the presence of the cardiac activity may be identified on MSE profiles of BP and LDF signals. GTN administration induces changes in control processes of BP signals and LDF signals recorded on the forearm. However, GTN has no significant impact on the irregularity of LDF signals from finger. Therefore, GTN impact may depend on anatomical sites. Further works could now be conducted on pathological subjects to enhance diagnosis.

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