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Influence of Autonomic Impairment on Blood-Pressure and Heart-Rate Scaling Structures

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Abstract— **Self similarity is a promising tool for quantifying alterations in cardiovascular dynamics, although the effect of the autonomic control on the scaling structure of cardiovascular signals is still unknown. To address this issue, we studied spinal-cord injured subjects as a model of progressively impaired vascular control. We considered 24 able-bodied subjects (AB) and 23 paraplegics with lesion at different levels: between T_{12} and L_4 (N=7); T_5 and T_{11} (N=9); and C_6 and T_4 (N=7). We recorded blood pressure and heart rate in three conditions characterized by increasing sympathetic activation: supine (SUP); sitting (SIT); and exercise (EXE). We calculated the scaling exponent of mean arterial pressure, H_{MAP}, and of R-R interval, H_{RRI}, by detrended fluctuation analysis. The sympathetic activation had different effects on the scaling exponent, depending on the lesion level. H_{RRI} did not change significantly from SUP to SIT and to EXE in the AB and T_{12}-L_4 group, while it increased in the T_5-T_{11} and C_6-T_4 groups. Also for H_{MAP} sympathetic activation produced changes which depend on the level of the spinal lesion. In particular, our results suggest that heart-rate self similarity depends on the vascular sympathetic control, because it is altered by the spinal-cord lesion even when the cardiac neural control is intact.**

I. Introduction

SPECTRAL analysis of heart rate and blood pressure beat-to-beat variability revealed important physiological and pathological aspects of the autonomic control of circulation. More recently, researchers also focused their studies on complex and nonlinear characteristics of these signals. In this context, a promising tool for better understanding the neural cardiovascular regulation is the assessment of signals self-similarity. In fact, fractal-like anatomical structures in the heart and vasculature, and complex interactions among vascular beds, suggest that cardiovascular signals are generated by fractals, self-similar processes [1,2]. Although it has been shown that self-similarity of heart rate may change with age or specific diseases [3], it is still unknown how the autonomic nervous system influences the scaling structure of the cardiovascular signals.

The lesion of the spinal cord is a pathophysiological model which may help to understand how sympathetic efferences on the heart and vasculature determine the scaling structure of cardiovascular signals. Patients with spinal cord injury experience loss of autonomic control of circulation below the lesion level. Their vascular autonomic control is impaired in vascular segments innervated by sympathetic pre-ganglionic fibers below the lesion level. If the lesion level is above the fourth thoracic vertebra, T_4, also the sympathetic outflows to the heart is partially impaired. Thus, the spinal cord lesion is a human model of intact vagal cardiac modulation, associated with the loss of sympathetic regulation of a number of sublesional vascular districts. Since the degree of impairment of sympathetic control depends on the level of the lesion, this condition may allow to investigate the contribution of the sympathetic vascular control on the scaling structure of blood pressure and heart rate.

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II. Methods

A. Subjects

We enrolled 23 paraplegic subjects and 24 healthy able-bodied, AB, volunteers. Paraplegic subjects were classified into three groups depending on the level of their spinal cord lesion: between the 6th cervical and the 4th thoracic vertebra, C_6-T_4 (N=7); between the 5th and the 11th thoracic vertebra, T_5-T_{11} (N=9); and between the 12th thoracic and the 4th lumbar vertebra, T_{12}-L_4 (N=7). Subjects in the T_{12}-L_4 group experience an impaired vascular control in the inferior mesenteric district only. The impairment affects also vascular districts innervated by the splanchnic nerve in subjects of the T_5-T_{11} group. Both T_{12}-L_4 and T_5-T_{11} groups have intact neural cardiac modulation. By contrast, subjects in the C_6-T_4 group are also characterized by a partially compromised sympathetic modulation of the heart. All

subjects underwent a thorough clinical examination before being enrolled in this study: exclusion criteria were the presence of any symptom or sign of cardiorespiratory disease or of other pathological conditions (like diabetes or hypertension) that might affect the autonomic cardiovascular control. Each subject gave informed consent to the experimental procedure, which was approved by the Ethics Committee of our Institution.

B. Experimental Protocol

In each subject, continuous arterial blood pressure at the finger artery (Finapres) and the ECG were simultaneously recorded for 10 minutes in three conditions: during supine rest (SUP); while sitting at rest (SIT); and during a light upper arm exercise performed on an arm ergometer (EXE). The order in which the three recordings were performed was randomized. These three conditions are characterized by a progressive activation of the sympathetic system, the lowest baseline value being obtained during supine rest. Beat-by-beat R-R interval values, RRI, and mean arterial pressure, MAP, were derived from each recording.

C. Assessment of scaling-exponents

A time series $x(t)$ is self-affine if it has the same statistical properties of $a^{-H}x(at)$ for any a greater than zero, and self-similar if the above relation holds for H equal to 1. Thus evaluating the self-similarity of a time-series implies the estimation of its scaling exponent H. The scaling exponents for mean arterial pressure, H_{MAP}, and for R-R interval, H_{RRI}, were estimated by means of detrended fluctuation analysis as described in [4]. First, we computed the integral of each series $x(i)$ after subtraction of its mean value:

$$y(k)=\sum_{i=1}^{k}\left(x(i)-\mu\right) \qquad (1)$$

with μ being the mean of $x(i)$. The integrated series was divided into boxes of equal length, n, and in each box a least-square line $y_n(k)$, representing the trend in that box, was fit to the data. Then the integrated series was detrended by subtracting the local trend. The root-mean square $F(n)$ of the detrended series:

$$F(n)=\sqrt{\frac{1}{N}\sum_{k=1}^{N}\left(y(k)-y_n(k)\right)^2} \qquad (2)$$

was measured in each box and plotted against the box size n on a log-log scale. The slope of the regression line between $log(n)$ and $log(F(n))$ gave the scaling exponents.

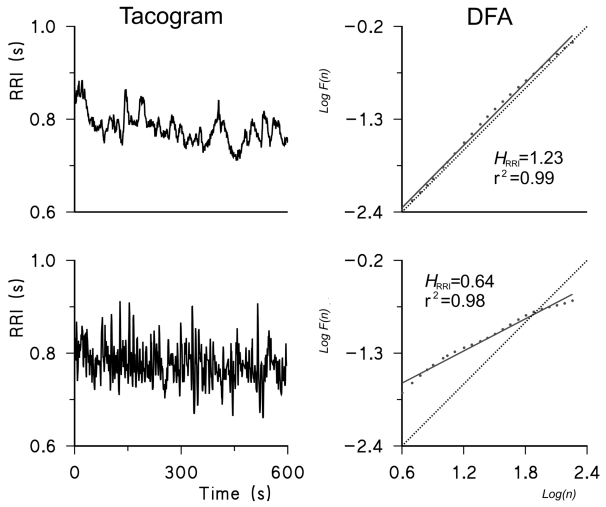

Fig 1. Example of evaluation of the exponents H_{RRI} by detrended fluctuation analysis in two RRI time series with very different scaling structures. Please note that in both cases the relation between $F(n)$ and n (see eq.2) is characterized by a very high linearity when plotted in a log-log scale.

D. Statistical Analysis

In each group of subjects, we tested the differences between the scaling structures of the two signals (H_{MAP} and H_{RRI}) and how the maneuver (change of posture and exercise) differently affect each scaling structure, by applying a repeated measures Analysis of Variance (ANOVA) with two level of repeated measures: type of signal (MAP or RRI) and maneuver (SUP, SIT and EXE). The Fisher LSD test was used for post-hoc comparisons. The level of statistical significance was set at $p<0.05$.

III. RESULTS

The four groups of subjects were matched in terms of body mass index and resting arterial blood pressure in sitting position. MAP values during each maneuver are shown in Table I, separately in each group.

TABLE I
MAP SEPARATELY FOR EACH GROUP OF SUBJECTS: MEAN (SEM)

	SUP	SIT	EXE
AB	86.0 (1.9)	92.5 (2.2)	98.0 (2.2)
T_{12}-L_4	99.0 (7.1)	98.5 (2.0)	104.2 (4.3)
T_5-T_{11}	82.8 (3.7)	92.0 (6.1)	105.1 (6.6)
C_6-T_4	73.8 (3.8)	88.1 (4.3)	88.4 (6.9)

values in mmHg.

Age was slightly but significantly higher in the T_{12}-L_4 group (38.4±9.3 yrs, M±SD) than in the other groups (AB: 29.7± 6.4; T_5-T_{11}: 31.0 ± 4.8; C_6-T_4: 25.6 ± 4.1). Mean values of RRI are reported in Table II.

TABLE II
RRI SEPARATELY FOR EACH GROUP OF SUBJECTS: MEAN (SEM)

	SUP	SIT	EXE
AB	953 (36)	832 (31)	742 (28)
T_{12}-L_4	888 (71)	846 (59)	749 (50)
T_5-T_{11}	862 (64)	772 (69)	634 (45)
C_6-T_4	973 (32)	891 (51)	735 (33)

values in ms.

Significances of each factor are shown in table III, separately for each group of subjects.

In the AB group, the type of signal is a largely significant factor: this means that the scaling structures of RRI and MAP differ significantly. Also the maneuver is highly significant, indicating that the scaling structure is influenced by the sympathetic activation induced by the change of posture and by exercise. The significance of the interaction between factors (Type x Maneuver) reveals that the sympathetic activation has different effects on H_{MAP} and H_{RRI}.

Figure 2 summarizes the results for the control group of able-bodied subjects. In controls, both blood pressure and heart rate scaling exponents decrease with the sympathetic activation induced by the change of posture and by the further activation caused by exercise. H_{MAP} is significantly greater than H_{RRI} in the condition with the lower sympathetic tone (supine). The increase in sympathetic tone has a greater influence on H_{MAP} than on H_{RRI}, and the difference between the two scaling exponents tend to decrease with the sympathetic activation.

Table III shows that the spinal cord lesion has important effects on both the scaling structures, and in the way they are modified by the sympathetic activation.

TABLE III
ANOVA: SIGNIFICANCE P OF EACH FACTOR SEPARATELY FOR EACH GROUP OF SUBJECTS

Group	Type of signal	Maneuver	Type x Maneuver
AB	**6×10^{-4}**	**1×10^{-5}**	**0.005**
T_{12}-L_4	0.09	0.51	0.61
T_5-T_{11}	**0.04**	0.94	**0.005**
C_6-T_4	**0.03**	0.14	**0.02**

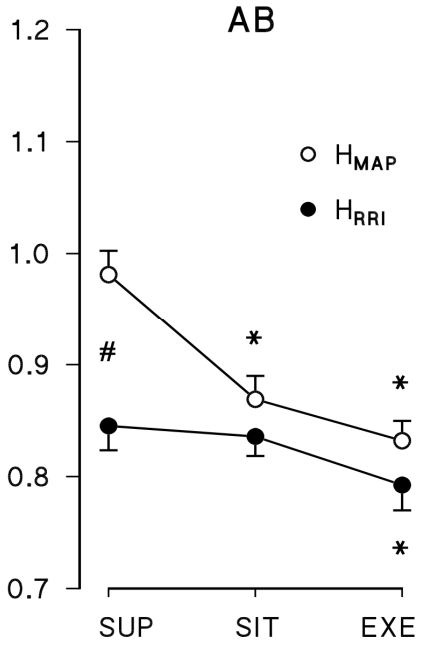

Fig 2. Scaling coefficients for MAP (open circle) and RRI (solid circle): mean and SEM in the group of able-bodied subjects during supine rest (SUP), while sitting at rest (SIT) and during a light exercise performed in sitting position (EXE). The * indicates significant differences vs. SUP; the # significant differences between H_{MAP} and H_{RRI}.

Differently than in controls, the manoeuvre is not a significant factor in spinal cord injured subjects. However, in paraplegic subject with the higher levels of lesion (T_5-T_{11} and C_6-T_4), this is due to the opposite effects that the sympathetic activation produces on the two scaling exponents, as indicated by a highly significant factors interaction. In particular, post-hoc analysis (fig.3) reveals that while H_{MAP} does not change (C_6-T_4) or significantly decreases (T_5-T_{11}) from supine to exercise, H_{RRI} significantly increases, shifting from mean values lower than 0.9 to mean values greater than 1. The increase was greater and more significant for the group with the higher lesion level.

As far as the group of paraplegic subjects with the lower lesion level is concerned, H_{RRI} and H_{MAP} values were similar among the three conditions.

A common features in the groups of spinal-cord injured subjects is that the difference between the two scaling exponents tend to vanish in parallel with the sympathetic activation, because H_{MAP} decreases when H_{RRI} increases.

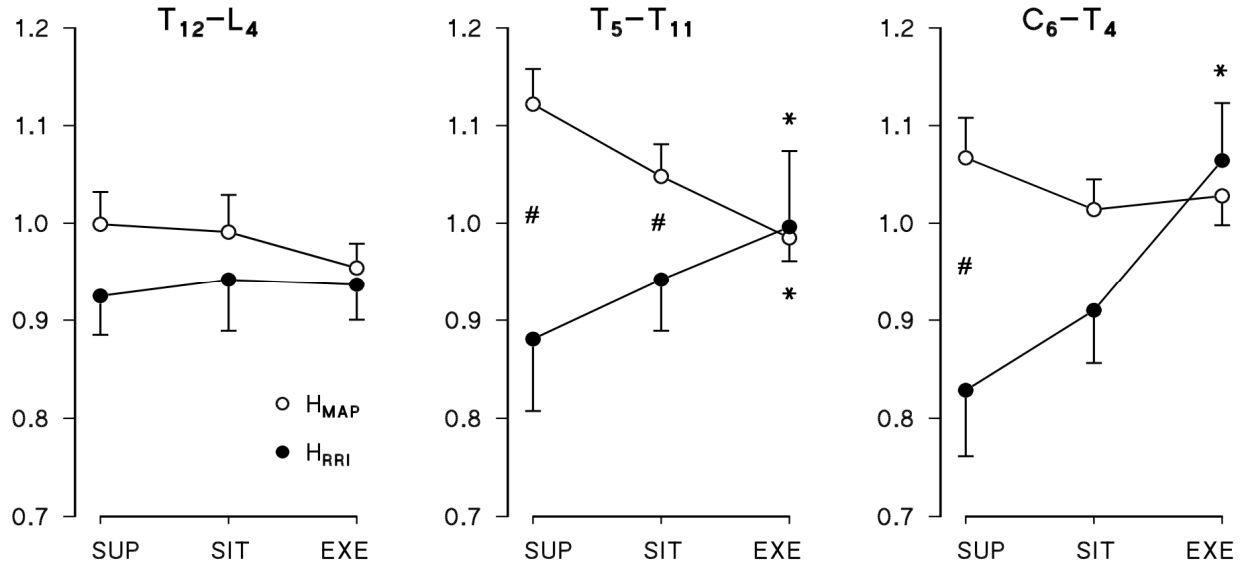

Fig 3. Mean value and SEM of scaling coefficients for MAP (open circle) and RRI (solid circle) in each group of subject affected by spinal cord lesion. Symbols as in figure 2.

IV. Discussion

Our study shows that the characteristics of blood pressure and heart rate self-similarity depend strongly on the sympathetic control. In particular, we showed that not only the MAP scaling structure, but also the scaling structure of heart rate depends on the sympathetic control on the vasculature, because H_{RRI} is altered by the spinal cord lesion even when the neural control of the heart is intact.

Our data indicate that in healthy subjects a sympathetic activation following a blood redistribution (due to a change of posture or to an augmented need for blood flow to the muscular districts) does not increase the long-term correlation of heart rate. This may be due to an efficient sympathetic vascular regulation, whose effect is to reduce H_{MAP} to values lower than 0.9 during SIT and EXE. Actually, long-term correlation of heart rate seems even to slightly decrease in the direction of white noise during exercise, the mean scaling exponent being reduced to 0.79.

By contrast, when the vascular regulation is partially compromised, it seems that the altered sympathetic control should be compensated by slow heart rate variability which increase the long term correlation in the direction of 1/f or Brown noises, also increasing the H_{RRI} exponent. In line with this hypothesis, we found that the H_{RRI} increase which follows the sympathetic activation is more marked when the lesion level is higher; and that the increase of H_{RRI} from rest to exercise seems less capable to reduce the H_{MAP} exponent in the group with the more compromised sympathetic activation, i.e., with lesion level between C_6 and T_4.

References

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