Cardiorespiratory coupling is influenced by body position and slow paced 0.1Hz breathing in a state specific manner

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Objective: Cardiorespiratory coupling (CRC), a set of cardiac and respiratory rhythms that optimise the body oxygenation and the adaptability of the cardiorespiratory system to the external and internal environment, is represented in the linear domain by pulse/respiration quotient Qpr, the number of heartbeats per respiratory cycle[1,2]. Slow 0.1Hz breathing in supine position (*supin01*) and active standing (*stand*) represent the states of maximal RRI vagal and sympathetic modulation, respectively, in physiological quiescence, while standing with 0.1Hz breathing (*stand01*) is characterized by by simultaneous sympathovagal enhancement.

The aim of our work was to investigate the linear CRC by Qpr in 4 states: supine position with spontaneous breathing (*supin*), *stand*, *supin01* and *stand01*.

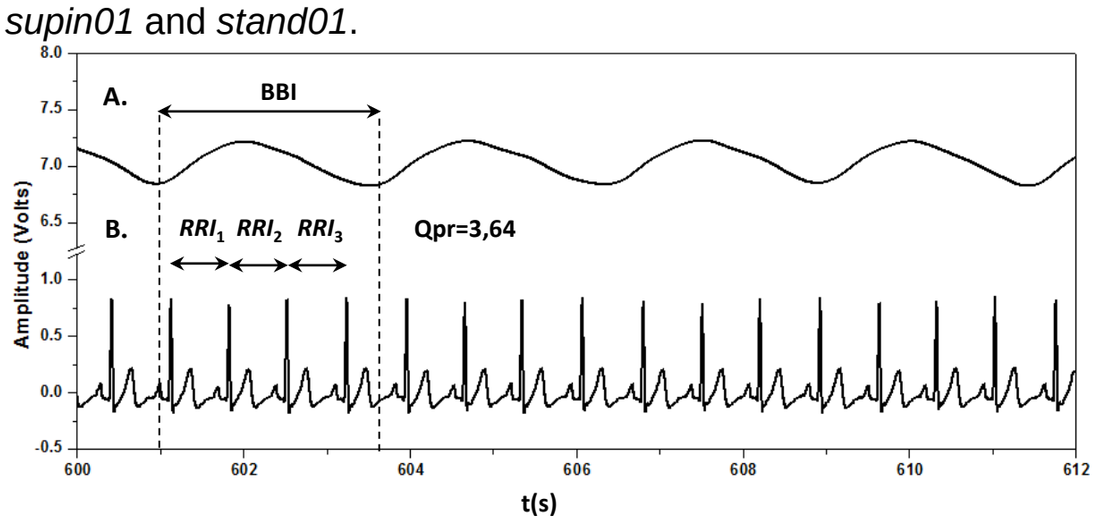

FIGURE 1. Segment of respiratory signal (**A.**) and ECG signal (**B.**) in one subject, recorded simultaneously, in a supine state with spontaneous respiration, for 12s selected from a total of 1200s registered in this condition.***RRI*** -time interval between two adjacent R peaks of ECG, ***BBI***- breath-to-breath interval, ***Qpr***- number of heart beats in one breath-to-breath interval.

Methods:

The ECG (RRI) and respiration signals were simultaneously recorded in 20 healthy human subjects in four conditions.

1. Subjects

We conducted the study protocol on 20 healthy adult human subjects (13 males, age 34.4±7.4) which was approved by Ethical Committee of Faculty of Medicine, University of Belgrade. Inclusion criteria: absence of any health problems and an age between 20 and 45 years. Exclusion criteria were: subjugation to any therapy (acupuncture, medications, etc); a history of cardiovascular, pulmonar or any other diseases; presence of any health disorders, at the time of the assessment, pathological symptoms during the experimental procedures. For female participants an additional criterium of exclusion was the second part of menstrual cycle . All participants were advised to refrain from food and drink about 4 hours before the experiment, not to exercise, to be restful and alert.

2. Study protocol

The study protocol was performed under controlled laboratory conditions at the Laboratory for biosignals, Institute for Biophysics, Faculty of Medicine, University of Belgrade. It was conducted in quiet, refreshing and constant temperature environment (22±1ºC). Experiments were undertaken between 8 and 12 AM[4]. All subjects were subjected to 10 minutes of relaxation in a supine position before recording. There was no restriction imposed on the air flow rate. They were also strictly instructed not to talk during the experimental procedures.The ECG (RRI) and respiration signals were simultaneously recorded in 4 conditions/sessions: supine and standing positions at spontaneous breathing rates,and in supine and standing positions with the slow paced 0.1Hz breathing rates. Session recordings lasted for 20 minutes, with a 5 minute pause between the supine and standing position, in order to meet the criteria for cardiorespiratory complexity analysis[5,6] and to obtain the stabilization of autonomic regulation in each state[4]. The sequence of these four sessions was randomly chosen. Slow breathing with a paced rhythm of 0.1 Hz was dictated by a computer web metronom (www.webmetronome.com). Subjects were trained and instructed for slow breathing regime before the recording sessions.

3. Data acqusition

ECG and respiration signal acquisition was done by means of Biopac MP100 system (Biopac System, Inc, Santa Barbara, CA, USA;AcqKnowledge 3,91 software). Main ECG lead registration electrodes were attached on the projections of clavicle bones and the grounding on the ancle of the right leg.The belt with resistive strain gauge transducer for continuous recording of breathing was placed slightly above the costal line. Both signals were sampled with 1000 Hz frequency rate.

4. Data processing

Respiration signal was low pass filtered (4th order Chebyshev filter)[7]. RRIs were extracted from the ECG signal using Pick Peak tool in Origin (Microcal, Northampton, MA, USA). Since the sample rate of the respiration signal was uniform (1000 Hz), while RRI values form signals with unequally positioned samples (sampling frequancy lower frequency than 1000 Hz) a resampling of respiration signal was performed, according to the samples of RRIs. It was done using our custom Matlab program[7].

X(i)=col(Pkx)[i+1]-col(Pkx)[i] **(1)**

col(Pkx)[i]- x (time) coordinate of marked signal point
col(Pkx)[i+1]- x (time) coordinate of subsequent marked signal point
X(i) - *RRI*(i) or *BBI*(i), with respect to the type of the signal

Qpr was calculated according to the following procedure (explained for the first breathing interval as an example). Suppose that respiratory and r peaks were arranged in the following order (i, e – points in time when inspiration and expiration started, respectively, r – occurrence of an ECG R peak):

Respiration e.....i1.....e.....i2.....
R peaks r0.....r1...r2 .....r3....r4...r5....r6
Number of intervals 1 2 3 4

First we counted integer number of whole r r intervals that fell between i1 and i2. In this case there were three of them: r2 - r1, r3 - r2 and r4 - r3.
Then parts of the boundary r r intervals that belong to (i1, i2) breathing interval, as non-integer parts of the Qpr, were added:

b1(i1,i2) = (r1 - i1) / (r1 - r0), and b2(i1,i2) = (i2 - r4) / (r5 - r4). **(2)**

Finally, total (integer and decimal) value of Qpr belonging to (i1, i2) breathing interval was calculated as

Qpr(i1,i2) = 3 + b1(i1,i2) + b2(i1,i2) **(3)**

Results:

Parameter	Supin (mean±95%CI)	Stand(mean±95%CI)	Supin01(mean±95%CI)	Stand01(mean±95%CI)
RRI [s]	0.98±0.13	0.72±0.10	1.06±0.13	0.75±0.09
sdRRI [s]	0.06±0.02	0.04±0.02	0.09±0.03	0.07±0.02
BBI [s]	4.68±1.53	4.58±1.80	9.85±0.71	9.95±0.20
sdBBI [s]	1.11±0.69	1.35±1.29	1.44±0.94	1.06±0.44
Qpr	4.81±1.67	6.39±2.43	9.41±1.20	13.48±1.66
sdQpr	1.14±0.67	1.93±1.73	1.39±0.71	1.54±0.53

Table 1. Mean value and 95% CI of RRI, BBI and Qpr for 20 healthy subjects in four physiological states: Supin-supine position with spontaneous breathing, Stand-standing with spontaneous breathing, Supin01-supine position with 0.1Hz breathing, Stand01-standing with slow 0.1Hz breathing.

Parameter	Supin-Stand	Supin-Supin01	Supin-Stand01	Supin01-Stand01
RRI	0.000 ↓	0.004 ↑	0.000 ↓	0.000 ↓
sdRRI	0.004 ↓	0.000 ↑	0.351 ↑	0.010 ↓
BBI	0.391 ↓	0.000 ↑	0.000 ↑	0.313 ↑
sdBBI	0.232 ↑	0.433 ↑	0.911 ↓	0.135 ↓
Qpr	0.000 ↑	0.000 ↑	0.000 ↑	0.000 ↑
sdQpr	0.006 ↑	0.370 ↑	0.033 ↑	0.191↑

Table 2. Probability values (p) of statistically significant differences between different physiological states. Wilcoxon test on a sample of 20 subjects. Color-indicated statistically significant changes in values ($p < 0.05$) whose changes were related and discussed. ↑ - increase of mean value, ↓ - decrease of mean value.

Conclusion: Our results show that linear CRC Qpr is state dependent and that it increases with the behavioral task complexity. Postural change tunes Qpr by RRI modulation, while 0.1Hz breathing dominantly by the increase of BBI. *Stand01* is characterized by concomitant reciprocal adjustment of both RRI and BBI. These data imply that Qpr regulation is "loosely" and selectively coordinated in *stand* and *supin01*("dual control") while integrated in *stand01* ("unitary control"[8]). Analogously to nonlinear CRC[3], **Qpr is probably operated in bottom up manner of brainstem and hierarchically higher forebrain-central autonomic networks with respect to the increment of behavioral complexity task**. In 0.1Hz breathing regimes (*supin01* and *stand01*) Qpr has higher values compared to the respective states with spontaneous breathing (*supin* and *stand*). These results support provocative hypothesis that **Qpr might be a promising marker of cardiorespiratory ventilation-perfusion efficiency**, specifically increased during slow 0.1Hz breathing. Further research on this hypothesis is necessary.

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T.B. acknowledges financial support from **FENS Grant and Voucher Program** and **Serbian Neuroscience Society**