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Physical fitness contributes to cardio-respiratory synchronization

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Abstract—Cardio-respiratory synchronization is a phenomenon of particular interest- especially at a 1:1 ratio- and may give greater insight into the underlying mechanisms of cardio-respiratory communication. Synchronization of this ratio is hypothesised to occur when breathing rate exceeds heart rate, which is the premise of this research. A novel experimental design focused on guiding elevated respiration to induce the entrainment of heart rate, and produce an equivalent rise in value. Application of instantaneous phase for identification and analysis of synchronization allowed for a reliable method of measuring the interaction between these stochastic processes. We have identified 1:1 phase synchronization in all volunteers measured. Longer synchronization episodes were observed reliably in athletic individuals, corroborating previous research for spontaneous breathing. This observation suggests that cardio-respiratory synchronization at all respiration rates is associated with a common underlying communication mechanism. Furthermore, it presents cardio-respiratory synchronization as a potential future measurement of fitness and autonomic health.

I. INTRODUCTION

Cardiac and respiratory systems are controlled by the autonomic nervous system and are necessary for appropriate gas exchange [1]. A strong coupling between cardiac and respiratory rates manifests itself as cardio-respiratory synchronization (CRS), with m heart beats occurring per n respiration cycles ($n : m$ locking ratio) [2, 3, 4]. Heartbeats are observed for explicit phases of the respiratory cycle during CRS. Therefore, recent advances have demonstrated the applicability of a phase description [5] of CRS. Previous research investigated CRS for respiratory rates less than heart rate, i.e. for $n < m$ [2, 3, 4].

The origin of the coupling experienced between cardiac and respiratory systems has been suggested to be peripheral as well as central [7]. Accordingly, CRS for low rate breathing is considered the product of peripheral coupling [8, 9], as the reaction time of systems is less than the period of respiration. Due to the proximity of respiratory and cardio control centres, it has been suggested that when the rates of the cardiac and respiratory systems are close in value, direct neural coupling should manifest [7]. Pokrovskii considered the response of heart rate to breathing at a rate exceeding resting heart rate (RHR) in a number of experiments [10]. They reported CRS at a 1:1 ratio, and suggested direct communication between neural centres in the medulla oblongata.

CRS for spontaneous breathing has been suggested to be more prominent in athletes [6, 11]. In fact, one of the first reported experiments [2] was carried out on a group of elite athletes, all being swimmers. Their specific training and the rhythmic nature of their sport was suggested to reinforce the strength of interconnection within the cardio-respiratory system. As athletes have superior lung capacity, respiratory musculature, and heart strength when compared to sedentary individuals [12], it is not clear whether the enhancement of coupling is mechanical, originating from greater forces from cardio-respiratory processes, or from a rhythmically trained interconnection between neural centres within the medulla.

This work aims to investigate 1:1 phase-locking CRS in healthy volunteers. Inspired by the conclusions of Pokrovskii's work [10, 13, 14], breathing will be guided at rates close to and exceeding RHR**.** A detailed description of these experiments and the results with corresponding statistical analysis are published in [15]. This article is looking to analyse the differences in length of synchronization for volunteers of different fitness capabilities. Specific subgroups are identified within the data, namely non-athletes, fit and athletes, and the differences between synchronization durations assessed. Furthermore, as HRV has been demonstrated for non-invasive monitoring and diagnosis of certain conditions, such as autonomic neuropathy [16] and prediction of chronic kidney failure [17], with further investigation it is suggested that identification of CRS could similarly have clinical potential, for characterising fitness, age or monitoring recovery from anaesthesia [14, 18, 19].

II. METHODOLOGY

A. Experimental setup and measurements

During this study, 22 volunteers took part in measurements, aged between 18 and 47 years. Ethical approval was granted by the Biomedical and Scientific Research Ethics Committee at the University of Warwick (REGO-2013-565). In conjunction with this, all volunteers provided consent to participate, after appropriate briefing.

A BIOPAC physiological signal monitoring system [20] was used for collecting ECG data, using limb lead electrodes, and breaths, using a respiration belt transducer. Signals were recorded simultaneously, at a sampling rate of 1000 Hz. As an autonomous process which can be controlled, breathing was chosen as the "driving force", with the coupling response of the heart being measured. To instigate 1:1 synchronization, respiration must equal or exceed RHR [10]. Owing to the stochastic nature of physiological signals, and the inherent randomness of breathing, a sinusoidal guiding metronome animation was designed to ensure a quasi-harmonic input signal. Volunteers were lying down throughout recording.

After arriving at the laboratory, up to 30 minutes was allocated to volunteers for resting, to help ensure RHR and breathing rates were as relaxed as possible. Averaging heart rate over the last 4 minutes of rest time determined the mean

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heart rate for metronome speed calculation. Experimental recording consisted of spontaneous breathing for 10 minutes, followed by three guided intervals of breathing at high-rates. The 1st guided interval required breathing at 90% of the RHR, the 2nd interval at a rate equal to the RHR, and the 3rd interval guided breathing at 120% of the RHR. Each interval lasted for 100 complete breaths. A 4-minute recovery followed each high-rate interval, to ensure a return to RHR.

66 individual guided intervals are considered, 3 for each of the 22 volunteers. To consider physiological differences, the volunteers have been divided into 3 subgroups. 9 volunteers practise a high level of physical activity, requiring rhythmic control of breathing, which in turn may enhance connections within peripheral control centres. Such activities include rowing, cycling, swimming, and weightlifting. The second group contained 7 volunteers who were fit, doing daily exercise, however their fitness was derived from disciplines with less regularity in rhythmicity of motion. This included high-level racquet-sport players. The remaining 6 volunteers described infrequent exercise or none.

B. Analysis

Physiological signals were post-processed, to remove interference and trends before identifying instantaneous breathing and heart rates. Instantaneous periods were identified via an event-based approach [2], through selection of R-peaks and breath maxima. Each output time moment t_i represents a heartbeat or breath, with the instantaneous period defined as $T_i = t_i - t_{i-1}$. Instantaneous rate was calculated as the reciprocal of period and further analysed for normality (Shapiro-Wilk test [21]) and stationarity (Kwiatkowski–Phillips–Schmidt–Shin test [22]), to investigate any significant changes during guided, high-rate breathing. Mean and variance were also calculated. An example of instantaneous rates for the three guided intervals is shown in Fig. 1.

The phase of heart rate, $\varphi_h(t_i)$, increases by 2π between consecutive R-peaks, and the phase at any time moment derived by linear interpolation. Identification of breathing maxima can lead to errors at high breathing rates. Therefore, after filtering the signal to remove noise, time-dependent phase of breathing, $\varphi_b(t)$, was calculated using the Hilbert transform. The instantaneous phase of each signal was used to calculate measures of synchronization to help quantify the strength of interaction at high-breathing rates. For initial identification of possible phase synchronization, a synchrogram [2] was used, where the relative phase $\Psi(t_k)$ of

Fig. 1: Instantaneous breathing rate (blue 'x') and heart rate (red '+') are shown for the three intervals of guided breathing. The "excessive" response of heart rate in interval 1 is particularly curious, and was not an unusual response within our data. Rate is shown in BPM.

fast (heart rate) and slow (breathing) signals was plotted, using the following expression: $\Psi(t_k) = \phi_l \mod 2\pi$, where ϕ_l is the phase of the breathing signal. 1:1 synchronization will be indicated by a single line within the plot.

Instantaneous phase difference $\varphi(t) = \varphi_h(t) - \varphi_b(t)$ was calculated between heart rate and breathing rate. During synchronization, the phase difference is nearly constant, and will be limited by 2π as one signal does not exceed the other by a complete period. To assign a value to duration of synchronization, episodes with phase difference $\varphi(t)$ less than 2π were determined. Individual episodes must exceed 5 seconds to be included as CRS.

To evaluate how close the phase difference is to a constant value, i.e. to characterise the strength of synchronization, synchronization index $\lambda(t)$ was considered [2]:

$$\lambda(t) = \sqrt{\langle \cos(\varphi(t))\rangle_t^2 + \langle \sin(\varphi(t))\rangle_t^2} \qquad (1)$$

Components in angular brackets were averaged over a 7-heartbeat time window, centred at time t. Where $\lambda = 0$, there is no coupling interaction. $\lambda = 1$ describes strong phase-locking between the systems, and constant phase difference. Being stochastic physiological signals, the phase difference between them will inherently fluctuate. Therefore an appropriate threshold of λ was derived experimentally. This was identified as $\lambda_{thr} = 0.7$ following analysis of synchrograms and synchronization index plots. For episodes exceeding 5 seconds where $\lambda \geq \lambda_{thr}$, synchronization was identified as a single episode of synchronization. Total duration of synchronization for a given interval of guided breathing was defined as sum of durations of single episodes.

III. RESULTS

A. Statistical Overview

Using guided breathing with an animated metronome, it was intended that heart rate would be subjected to a regular, constant "driving force". However, natural disturbances to the respiratory cycle inhibit this intention. The consideration of variability of the breathing rate during guided high-rate intervals gives insight into how effectively volunteers followed the metronome. The boxplots of breathing and heart rates for one volunteer are shown in Fig. 2. Values of rates in the figure have been normalised to RHR, thus the median value for interval 2 should show normalised breathing rate of approximately 1. Correspondingly, interval 1 and 3 should have normalised values of 0.9 (90%) and 1.2 (120%), respectively. Deviation of the breathing rate from the median within the cohort is around 5%. Upper and lower adjacent values were less than 10% of the median, justifying the selected step changes in guided breathing rates as distinct rates between intervals. Half (33 out of 66) of the elevated breathing intervals were identified as normally distributed, using the Shapiro-Wilk test. Using the KPSS test, 63 of the 66 intervals were identified as trend-stationary. This emphasises the breathing rate is mean-tending, oscillating in value around the desired rate. The breathing signal can be described as quasi-harmonic, with amplitude constant and frequency varying.
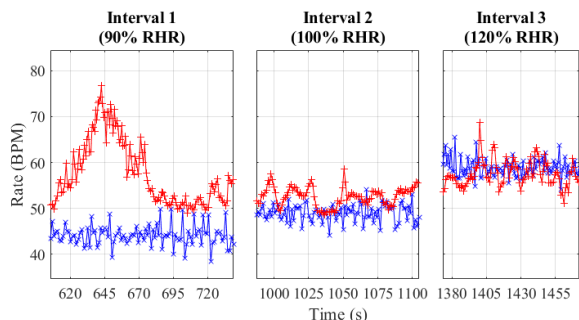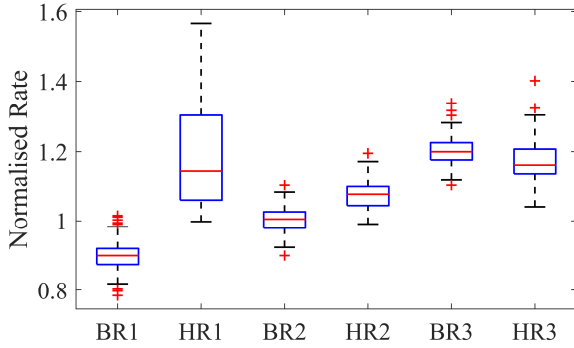
Fig. 2: Boxplots of normalised breathing rates (BR) and heart rates (HR) for one volunteer, for the intervals of guided, high-rate breathing (1, 2, or 3).
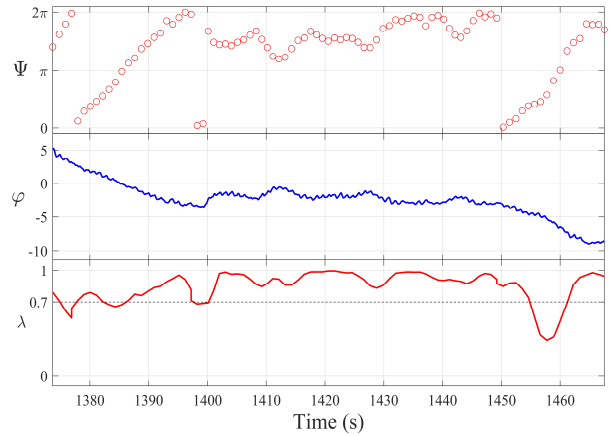

Fig. 3: Synchronization measures for one volunteer. The top panel shows the synchrogram; phase difference is shown in the second panel; the third panel has synchronization index in red, while the dashed line is $\lambda_{thr} = 0.7$.

During episodes of synchronization, heart rate dynamics would be expected to behave similarly to breathing rate. However, due to natural fluctuations, and the impact of other regulatory systems on heart rate, the overall picture is much more complicated. Therefore, it is not altogether surprising that variability of heart rate is greater than breathing rate, owing to these natural fluctuations, and overall control of the cardiac system being autonomic. Heart rate during intervals of high-rate breathing was non-normal in 75% of intervals (49 of 66), most likely due to the heart's adaptive, transient response to the step change in breathing (Fig. 1, interval 1, red line). 63 of 66 intervals were non-stationary, demonstrating wandering dynamics of heart rate [23]. Boxplots for normalised heart rate shown in Fig. 2 are labelled as HR.

B. Synchronization analysis

Following visual inspection of a synchrogram for each interval of guided breathing, regions of 1:1 synchronization were identified. For 18 of the 22 volunteers, CRS was observed during the 3rd guided interval, corresponding to a breathing rate exceeding RHR. For the other 4 volunteers, 1:1 CRS occurred during the 2nd high-rate interval, intended to be breathing at a rate equivalent to RHR. It is possible that the value used to determine the metronome rates was too high, and thus the second interval would also correspond to a breathing rate exceeding RHR for these individuals.

In Fig. 3, the measures for characterising phase synchronization are shown. The upper panel shows the synchrogram. Values of Ψ_k form a plateaued line visible between 1400 and 1450 seconds represents the relative phase between cardio-respiratory systems not changing or remaining limited. Following the criteria in the Methodology section, CRS was formally identified by regions where phase difference was limited by 2π, and synchronization index exceeded the derived threshold value, $\lambda_{thr} = 0.7$. Using these techniques, in many cases, more than one episode of CRS was observed within the same interval of guided breathing. As previously stated, an individual episode must exceed 5 seconds. The longest episode was highlighted, and the total duration of all episodes greater than 5 seconds in the given interval was also calculated. For the plateau visible in panel 1 between 1400-1450 seconds (Fig. 3), the behaviour of the

other two plots supports the identification of synchronization. In the middle panel, phase difference is limited, and almost constant. The synchronization index in the lower panel is above the threshold line, $\lambda_{thr} = 0.7$, for the same duration. The lower panel also clearly shows multiple episodes of $\lambda \geq \lambda_{thr}$.

For most volunteers, the longest single episode of CRS was significant, with durations ranging between 20 and 80 seconds. The summary of durations (in seconds) are presented in Fig. 4. Duration identified on the base of limited phase difference are the three left-most boxplots, and on the base of the synchronization index are the three right. Subgroups non-athlete (N-A), fit (F), and athlete (A) are displayed.

The CRS durations calculated by the two identification methods show similar durations within subgroups. Using the Wilcoxon rank-sum test at 5% significance level, statistical similarity was assessed between subgroups. The athlete and fit subgroups are similarly distributed, with no statistical difference observed for either measurement technique. Therefore, P-values for these comparisons are omitted from Fig. 4. The durations of synchronization for the non-athlete subgroup are clearly shorter, both in terms of total duration and longest single episode. Analysis of the corresponding P-values demonstrates a statistically significant difference between non-athletes and athletes for all comparisons, except longest single episode of $\lambda \geq \lambda_{thr}$. Comparison of durations for non-athlete and fit subgroups is not statistically significant. However, for comparisons of total duration of CRS for non-athlete and fit subgroups, it can be noted that P-values are boundary values (0.0793 and 0.0513 respectively).

The apparent difference between non-athletes and fitter individuals suggests that overall autonomic health enhances CRS phenomena more than specific training disciplines. It should be noted that the design of the experiment leads to a biasing problem. Most athletes and fit volunteers had lower RHR. Therefore, the metronome rates for guiding breathing would be inherently lower, and easier to achieve. However, it is clear that these people ought to be more capable of physical exertion for extended periods. This may have enhanced the synchronization durations for fitter volunteers.
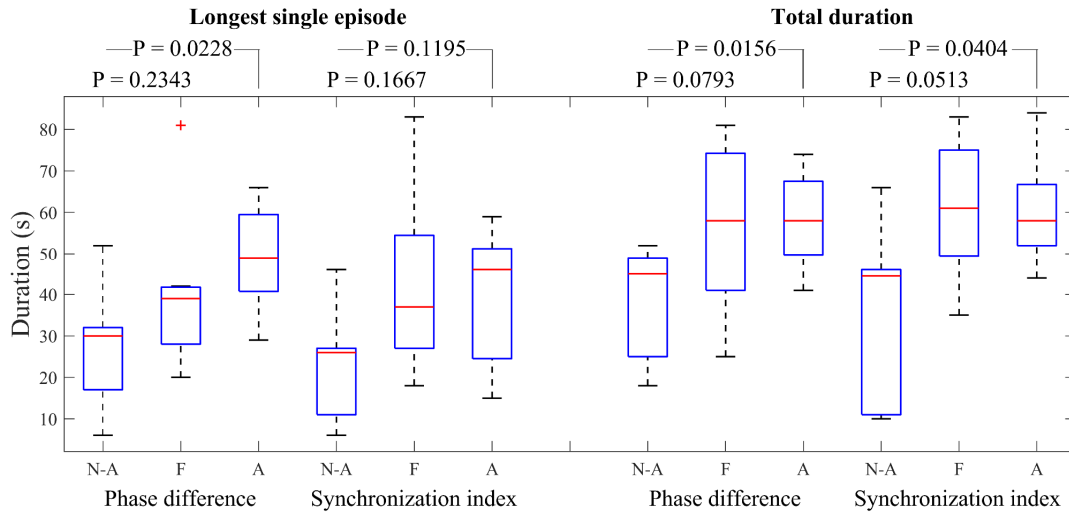
Fig. 4: Boxplots for synchronization durations for all volunteers, shown in seconds. Durations for $\varphi(t) < 2\pi$ and $\lambda \geq \lambda_{thr}$ are given for total duration (left-hand plots) and longest single episode (right-hand plots). The volunteers' results are displayed in the three subgroups- non-athlete (N-A), fit (F), and athlete (A).

IV. CONCLUSION

Both synchronization index and bounded phase difference have identified one episode of 1:1 CRS in all 22 volunteers at breathing rates equal to or greater than RHR, with high correlation between these methods and the synchrogram plots. Observation of CRS phenomenon when breathing rate exceeds RHR is in agreement with suggestions from previous research [10]. However, variability in results from this research shows a more complicated picture of cardio-respiratory interaction than previously reported [10, 13, 14], wherein the duration of synchronization was identified by visual inspection of signals.

Differences between athletes (volunteers who perform high-intensity exercise requiring rhythmic control of breathing) and non-athletes are statistically significant. This presents an area of possible applicability. The difference between non-athlete and fit subgroups is not as apparent as for non-athlete and athlete. Despite this, athlete and fit subgroups demonstrate similar durations of CRS. If individuals of generally higher fitness and autonomic health demonstrate longer CRS episodes, there is the potential to utilise this non-invasive technique for measuring a person's physical health. Furthermore, much as HRV has become a tool for measurement of autonomic health [24], greater understanding of CRS and its origins may lead to additional information regarding an individual's cardio-respiratory condition.

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