Interactions between cardiac, respiratory and brain activity in humans

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Abstract: The electrical activity of the heart (ECG), respiratory function and electric activity of the brain (EEG) were simultaneously recorded in conscious, healthy humans. Instantaneous frequencies and phases of the heart beat, respiration and α-waves were then determined from 30-minutes recordings. The directionality of coupling was then ascertained, using pairs of instantaneous frequencies in each case. It is shown that the systems are weakly bidirectionally coupled. It was confirmed that, in conscious healthy humans, respiration drives cardiac activity. We also demonstrate from these analyzes that α-activity drives both respiration and cardiac activity.

Keywords: synchronization, coupled oscillators, direction of coupling, α-waves

1 Introduction

It has long been known that the cardio-respiratory interaction provides the principal mechanisms giving rise to heart rate variability. More recently, it has been shown that the cardiac and respiratory systems can also synchronize and that, although the coupling is bi-directional, in conscious humans it is respiration that imposes the stronger influence rather than vice versa [7].

Much attention has been devoted to studies of nonlinear cardio-respiratory phenomena in humans. The deterministic character of the cardio-respiratory interaction is now well established in the waking state [9, 1], and in anaesthesia, both in humans [2, 3] and animals [10]. Considerable attention has been given to the analysis of EEG data during anaesthesia, based on a variety of methods [8]. Despite the extensive investigations of interactions between cardiac and respiratory oscillations, however, their interactions with brain waves have not hitherto been studied.

We investigate the interactions between cardio-respiratory system and α-waves in the EEG signal recorded from the forehead in conscious healthy humans. The causalities of the interactions are studied by calculating the directionality indices between all combinations of two signals and surrogate data [5] are used to test the significance of the results.

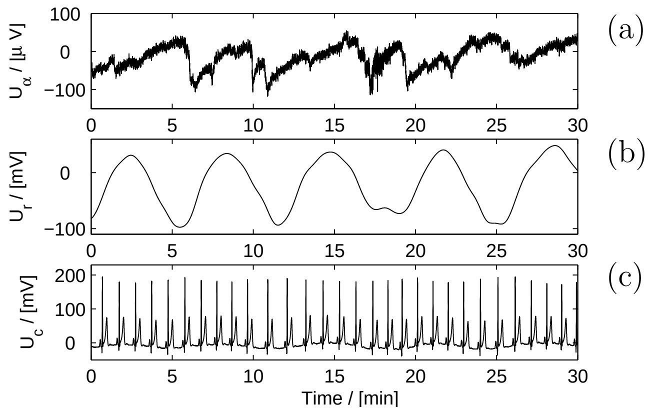

Figure 1: Extracts from the preprocessed time series. (a) electroencephalogram (EEG), (b) respiratory signal and (c) electrocardiogram (ECG).

2 Methods

Interactions between two systems can be described in many ways, here we will describe the method that is commonly used for the identification of causal relationships between two nonlinear oscillators. The method has its background in information theory [7], and the basic idea lies in making an estimate of how much information is contained in one oscillator about the other one.

This method relies on an estimate of information transfer between the two coupled oscillators [4, 6, 7]. Tools such as entropy $H(X)$, mutual information $I(X, Y)$ and conditional mutual information $H(X, Y|Z)$ are used. Suppose we have two stationary ergodic stochastic processes $X(t)$ and $Y(t)$. Simple interactions between these two systems can be studied by calculating the mutual information $I(y(t); x(t)_\tau)$, where $x_\tau(t) = x(t+\tau)$ and $y(t)$ are realizations of the two previous processes $X(t)$ and $Y(t)$, respectively. To extract the causality one has to use e.g. the conditional mutual information $I(x; y_\tau|y)$ and $I(y; x_\tau|x)$. This idea can be applied to a system of two coupled oscillators where the instantaneous phases ϕ_1 and ϕ_2 can be regarded as realizations of the processes $X(t)$ and $Y(t)$. Again in analogy with the previous method we consider phase increments

$$\Delta_{\tau,\phi_{1,2}} = \phi_{1,2}(t+\tau) - \phi_{1,2}(t). \tag{1}$$

To calculate the cross-dependencies we consider conditional mutual information $I(\phi_1, \Delta_{\tau\phi_2}|\phi_2)$ and $I(\phi_2, \Delta_{\tau\phi_1}|\phi_1)$ or, expressed more succinctly, $i(1 \to 2)$ and $i(2 \to 1)$. To obtain a normalized indicator, we compute a directionality index as in the previous case [7]

$$d_{1,2} = \frac{i(1 \to 2) - i(2 \to 1)}{i(1 \to 2) + i(2 \to 1)}. \tag{2}$$

3 Results

The experiment was performed at a constant room temperature (23 ± 1)°C. Data were obtained from a group of twelve adult male between 25 and 40 years old. The subjects were lying during the measurements and were asked to relax but stay awake. Three signals were measured and

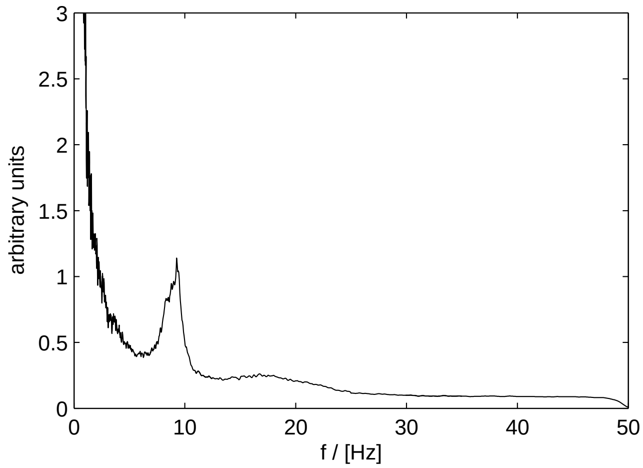

Figure 2: The time averaged wavelet transform, one can observe a pronounced spectral peak in the α region i.e. between 7.5 Hz and 12.5 Hz of the spectrum. This region was used to construct the band pass filter and to construct the phases of the signal.

recorded simultaneously on each subject EEG (a standard ZipPrep electrode used for depth of anæsthesia assessment based on BIS approach[8] was placed on subject's forehead), ECG and respiratory effort (measured with a inductive sensor placed on belt, which was placed over the subject's chest). The duration of the experiment was 30 minutes, all three signals were measured using signal conditioning unit (CardioSignals — designed at the "Jožef Stefan" Institute, Ljubljana, Slovenia) and digitized (16–bit resolution and 1kHz sampling rate) and stored on-line on a PC.

The data had been preprocessed to remove any trends that were present (see figure 1), then the frequency bands of all three signals had to be determined. For ECG and Respiratory signal this was relatively straightforward, on the other hand different approach was taken with the EEG signal. Its power spectrum has conventionally been divided into several frequency bands, defined as: δ (0.5–3.5 Hz), θ (3.5–7.5 Hz), α (7.5–12.5 Hz), β (12.5–25 Hz), γ_1 (25–35 Hz), γ_2 (35–50 Hz), γ_3 (50–100 Hz). Then, after filtered out low frequency trends, we applied wavelet transform. Because the α-frequency band contained the highest peak in the time-averaged wavelet transforms of the EEG signal in all subjects we concentrated our further analysis on it. The scalogram is presented in figure 2, where a pronounced peak is visible between 7 and 10 Hz. Although the scalogram does not show time localization of spectral component it gives better frequency resolution at lower frequencies, which hinders Fourier transform. This is important for detection of any possible lower frequency components.

The preprocessed signals were used to calculate the instantaneous phases. In the case of respiratory and EEG signals the Hilbert transform was used, while for the ECG the equation $\phi(t) = \frac{t_k - t}{t_k - t_{k-1}} + 2k\pi$ was used, where t_k is the time of the k-th peak.

Next, the interactions between the α-waves, cardiac and respiratory oscillators were studied with the directionality indices, which were calculated with the method described in previous section. The results are shown on figure 3, where all three possible combinations of signals are depicted. The indices (solid line) are drawn together with indices calculated from surrogate data (dotted line) to get the significance level. The cardio-respiratory directionality index

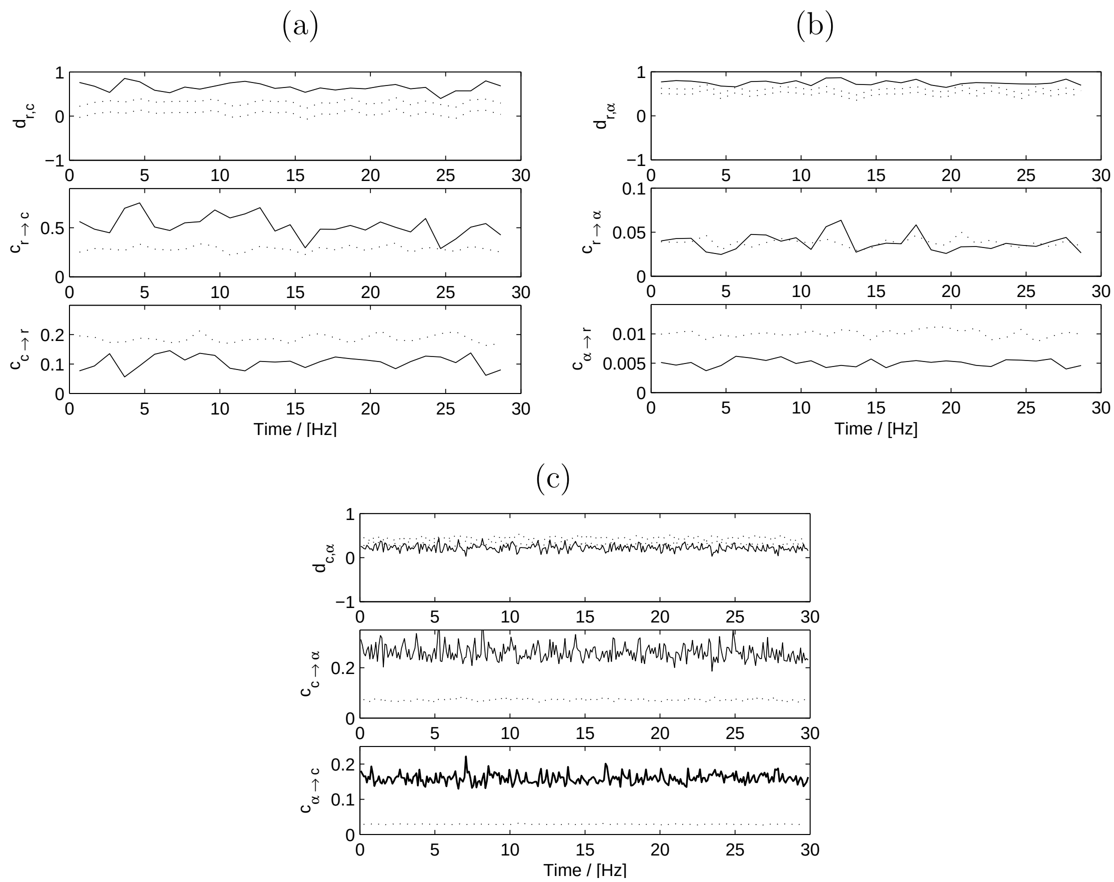

Figure 3: Directionality indices calculated between different combinations of two phases. (a) top panel shows the evolution of directionality index for cardio-respiratory system. The index is positive, which indicates that respiration is driving the cardiac. (b) depicts the evolution of directionality index calculated between respiratory and neural phases and is negative, which indicates that neural activity is driving the respiration. (c) directionality index calculated between cardiac activity and neural waves is negative, which indicates that neural activity is driving the cardiac or at least has effect on its dynamics.

	1	2	3	4	5	6	7	8	9	10	11	12
$d_{r,c}$	0,541	0,378	0,651	0,402	0,224	0,507	0,249	0,443	0,332	0,091	0,367	0,031
$c_{r\to c}$	0,620	0,382	0,524	0,314	0,445	0,395	0,324	0,425	0,318	0,304	0,478	0,281
$c_{c\to r}$	0,179	0,171	0,107	0,133	0,279	0,129	0,195	0,160	0,160	0,255	0,218	0,262
$d_{r,\alpha}$	0,698	0,642	0,749	0,707	0,544	0,705	0,598	0,657	0,636	0,550	0,644	0,518
$c_{r\to\alpha}$	0,040	0,033	0,038	0,034	0,033	0,033	0,031	0,032	0,032	0,032	0,031	0,032
$c_{\alpha\to r}$	0,007	0,007	0,005	0,005	0,009	0,005	0,007	0,006	0,007	0,009	0,006	0,010
$d_{c,b}$	0,212	0,238	0,238	0,240	0,230	0,217	0,227	0,248	0,254	0,244	0,223	0,248
$c_{c\to\alpha}$	0,270	0,259	0,260	0,264	0,270	0,270	0,258	0,265	0,263	0,255	0,273	0,267
$c_{\alpha\to c}$	0,169	0,154	0,154	0,155	0,163	0,168	0,156	0,153	0,150	0,149	0,168	0,154

Table 1: The mean values of all three combinations of directionality indices calculated for all 12 subjects. First two directionality indices ($d_{r,c}$ and $d_{r,\alpha}$) show that the respiration was driving the cardiac and the α-waves. The last index $d_{c,\alpha}$ indicates driving from cardiac to α-waves.

(top left) is positive and outside of region of surrogates. Both dotted lines depict ±1 standard deviation. The mean level of surrogates was calculated from 32 sets of surrogate data generated from the measured signals. Positive value of directionality index indicates that respiration is driving the cardiac, this is also visible from both partial indices ($c_{r\to c}$ is above the level of surrogates and $c_{r\to c}$ is below the level of +1 standard deviation of surrogates). The results from respiratory and α-waves interactions are similar except that the values of partial indices are lower, which indicates that the driving is present but is weaker. Finally, cardiac oscillator is driving the neural activity, where the difference between indices and their surrogates is well expressed. The results are illustrated only for one subject and summarized in table 1 for all remaining subjects.

4 Conclusion

In this study we demonstrated that causalities between cardio-respiratory oscillations and brain waves exist. This was achieved by comparing the values of directionality indices with the ones obtained from surrogate data. The directionality indices $d_{r,c}, d_{r,n}, d_{c,n}$ show that respiration is driving the cardiac and α-waves, while the latter two are coupled bidirectionally. The results have implications in future studies, where they can be used as a control group in a larger study in which different states of the system will be studied, e.g. anaesthesia.

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