

Short-Term Dynamics of Relative Coordination between Respiratory Movements, Heart Rate and Arterial Pressure Fluctuations within the Respiratory Frequency Range

U. ZWIENER, C. SCHELENZ¹, S. BRAMER, D. HOYER

Institute of Pathophysiology, and ¹Clinic of Anesthesiology and Intensive Care, Friedrich Schiller University, Jena, Germany

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Summary

The possible linear short-term coordination between respiratory movements (RESP), heart rate fluctuations (HRF), and arterial blood pressure fluctuations (BPF) in conscious human beings has not yet been investigated because of the restricted time resolution of conventional time series analysis. At present, this short-term dynamics as an expression of relative coordination can be quantified by newly developed adaptive autoregressive modeling of time series using Kalman filtering. Thus, in 6 conscious healthy volunteers, RESP, HRF, and BPF were recorded during 10 min in the supine position, at rest and during paced breathing. A considerable part of calculated ordinary and partial coherence sequences of short-term resolution between RESP and HRF, RESP and BPF, and partially between HRF and BPF showed patterns varying in time that could be correlated to changes between gradual coordinations (coherence changing between 0.40 and 0.95). They were more seldom complete or absent. There were mostly opposite changes between partial coherence sequences RESP-HRF/BPF and RESP-BPF/HRF demonstrating competitive behavior between these coordinations. Paced breathing did not essentially affect any observed characteristics. Therefore, these coherence dynamics are not essentially dependent on voluntary breathing movements. We conclude that to a different extent these linear and changing couplings between RESP, HRF, and BPF in conscious human beings exhibit properties of short-term complete and more frequently gradual coordinations showing dynamics that can not be determined by conventional methods.

Key words

Relative coordination • Coherence of short-term resolution • Partial coherence • Respiratory movements • Heart rate fluctuations • Arterial blood pressure fluctuations

Introduction

Some available results suggest that short-term changes of linear coordination occur between respiratory activities, heart rate fluctuations (HRF), and arterial blood pressure fluctuations (BPF) in mammals (Barman and Gebber 1976, Koepchen *et al.* 1981, Castiglioni *et al.*

1992). However, short-term quantification of these coordinations has never been performed.

Concerning the physiological background of these processes, Barman and Gebber (1976) described different degrees of synchronization between peripheral sympathetic and phrenic nerve activity that changed in a short-term manner from complete synchronization to a

“dissociation” state. Koepchen *et al.* (1981) and Langhorst *et al.* (1983) described “sliding coordinations” between respiratory and cardiovascular rhythms. Koepchen *et al.* (1981) found that these obey the rule of “relative coordinations” first detected by von Holst (1939) in motor rhythms of fish. These can also be found in cardiorespiratory coordinations. Erich von Holst defined “relative coordination” as concurrent nervous activities which function neither completely independently of each other nor in a fixed mutual relation. Presumably, the common mechanisms are the dynamics of neuronal networks such as those within the brainstem (von Holst 1939, Barman and Gebber 1976, Koepchen *et al.* 1981). The functional significance was stressed in changing gradual coupling for short-term tuning between respiratory and cardiovascular function in complex biological situations (Barman and Gebber 1976, Koepchen *et al.* 1981).

As far as the relative coordinations of longer duration are concerned, Fišer *et al.* (1978) were the first who demonstrated these phenomena between pulse intervals and diastolic blood pressure fluctuations in a coherence study.

We hypothesize that time-related patterns of short-term “relative coordination” also exist in awake humans, e.g. between respiratory movements (RESP), HRF and BPF. However, the quantification of these coordination dynamics requires (i) analysis with a temporally high resolution within the analyzed sequence of autonomous time series, and (ii) restriction of the analyzed coupling to that directly existing between two time series, i.e. excluding a concomitant influence of the third series. This can be achieved by partialization in the coherence calculation. The simultaneous calculation of ordinary and partial coherence between autonomous time series is well known (Gebber *et al.* 1994a,b).

Currently, such high-resolution analysis seems to be possible by the determination of “instantaneous” spectral power density and coherence by adaptive autoregressive modeling of time series using Kalman filtering (Arnold *et al.* 1998). The autoregressive coefficients are related to the spectral density by z-transformation. In this way, nonstationary time series can also be analyzed. Using this method, Arnold *et al.* (1998) have shown such short-term changes of linear coordination between RESP, HRF and BPF in anesthetized piglets 10-20 s after the onset of hypoxic hypoxia. The adaptation constant was chosen according to the physiological short-term dynamics of HRF, BPF

and RESP, such as the 10 s BPF and slower fluctuating processes.

We thus used the above possibilities and determined the ordinary and partial coherence of short-term resolution between RESP, HRF and BPF in healthy volunteers. In this way we could calculate the sequence of short-term coordination and compare the direct coordination determined by partial coherence between these three time series with the whole coordination including additional indirect influences upon the coordination caused by the respective third autonomous time series.

Thus, we can decide whether our hypothesis is true or not. To clarify whether voluntary breathing essentially influences such dynamics, we also analyzed the same parameters recorded during paced respiration.

Methods

Six young healthy volunteers of both sexes (23-34 years old, 3 males and 3 females) were examined between 9:00 and 14:00 h. All subjects were without medication and had had a sufficient night's sleep. The subjects were first instructed regarding the methods and aims of the study. Their chest-ECG was then recorded in supine (30°) position for 20 min. The arterial blood pressure was measured from the middle finger by vascular unloading technique known also as “volume clamp method” (Finapres 2300®, Ohmeda) (Peñáz 1973, Molhoek *et al.* 1984, Imholz *et al.* 1988). Blood pressure and respiratory movements (by impedance respirography) were registered at rest for 10 min and then during 10 min of paced respiration at constant frequency close to the mean rate of spontaneous breathing. This frequency was chosen to have similar conditions in both spontaneous and paced breathing except for the voluntary activity in the latter case. The pacing was indicated by a moving point of light on a PC screen to exclude effects of sudden clicks of a metronome in the sense of autonomous startles. In an earlier study (unpublished results), the tidal volume was spontaneously regulated by the subjects to a normal $p_a\text{CO}_2$. Therefore, we did not measure nor maintained a constant tidal volume to exclude the influence of the measurements on the studied subjects. The ECG was obtained with a standard AC amplifier, and care was taken to record an analogue signal with a prominent and positive R-wave that substantially reduced the likelihood of errors in the following steps. The ECG was fed through an A/D converter at a sampling rate of

1024 Hz to the mass memory of a PC (for further details see Zwiener *et al.* 1995, 1996a,b). The individual R-waves with the steepest R-wave rise, taken as the fiducial point, were then sequentially recognized. The reciprocal value of these series represents the instantaneous heart rate sequence. Artifact-corrupted data were rejected completely. The instantaneous heart rate sequence was resampled at 128 Hz. Before resampling, the reciprocal RR-intervals were linearly interpolated by a step function and consecutively low pass filtered (phase correct FIR-filter).

The traces of RESP and mean arterial pressure were sampled at a sampling rate of 128 Hz.

Data analysis

This instantaneous heart rate sequence was preprocessed with a 2 Hz low pass filtering by a FIR-filter system (Kornmüller 1991). A resampling rate of 8 Hz was chosen according to the anti-aliasing sampling theorem (Zwiener *et al.* 1995).

A trivariate autoregressive model of order 22 with time-varying coefficients was fitted to the simultaneous measured signals as described by Arnold *et al.* (1998). Thus, by means of the Kalman algorithm, the multidimensional processes of RESP, HRF and BPF were modeled as a multivariate autoregressive process with time-dependent coefficients. A sequence of spectral density matrices results from the sequence of autoregressive coefficients (Arnold *et al.* 1999). The resulting time-depending sequence is considered as a short-term estimation of spectral power and coherence. Investigations concerning the model order were performed by means of Akaike's information criterion (Chen and Guo 1991). The time resolution of the coherence curves is based on the recursive filter algorithm. Filters of order 22 were used. This means that 22 preceding samples are used in each iteration step, i.e. a time of $22 \times 0.125 \text{ s} = 2.75 \text{ s}$. Due to this recursive algorithm, further preceding data points are considered with decreasing weights. Consequently, 2.75 s plus adaptation time is here the coherence time resolution which is practically always smaller than 10 s. This is a sufficient time resolution with regard to the cardiorespiratory dynamics investigated.

The spectral parameters for calculation of ordinary and partial coherence of high time resolution were computed for the three possible pairs of RESP,

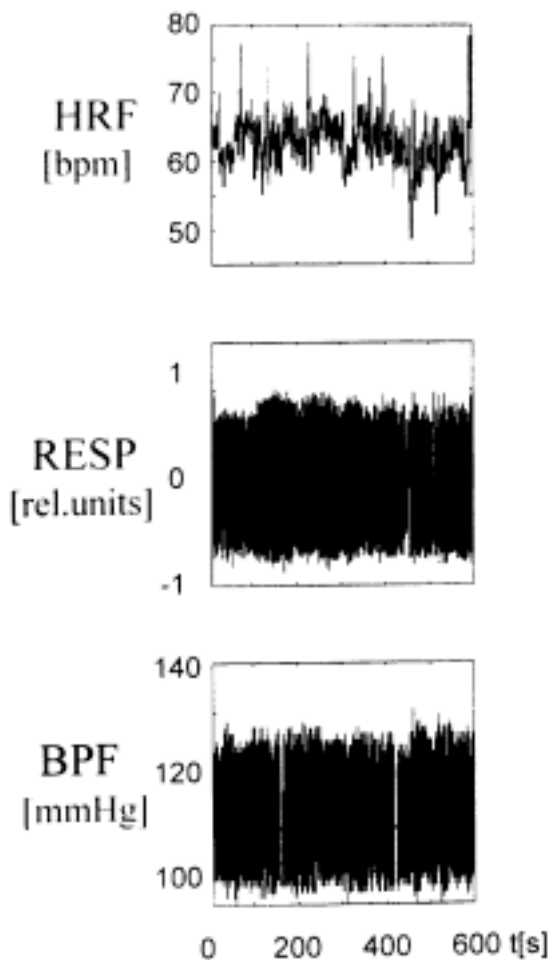


Fig. 1. Original recording of instantaneous heart rate fluctuations (HRF, in beats per minute), respiratory movements (RESP in relative units), and arterial blood pressure fluctuations (BPF in mm Hg) of a 30-year-old healthy male volunteer at rest. (From 163 to 167 s and 418 to 422 s autocalibrations of arterial blood pressure; the short-term coherences between BPF and the other autonomous time series are not certain here. This was taken into account for the coherence pattern analysis.)

HRF, and BPF (further details see Arnold *et al.* 1998). Ordinary and partial coherence was computed with the same windows and with the same resolution. Ordinary coherence was calculated as shown by Bendat and Piersol (1986) and Gebber *et al.* (1994a). Partial coherence includes the elimination (partialization) of that part of each of two signals that is determined by the influence of a third signal and the computation of coherence between the residual parts of the first two signals.

The abbreviations of ordinary and partial coherence were chosen according to Gebber *et al.* (1994a), for instance RESP-BPF for ordinary coherence,

but for partial coherence with the addition of the eliminated third time series here, e.g. RESP-BPF/HRF.

From all these ordinary and partial coherence values within the frequency band of respiratory movements, the maxima were chosen to build the continuous sequence of maximal coherence with short-term resolution as is shown in Figures 2-4.

Up to now there are no methods available for statistical assessment of significant differences between coherence values with short-term resolution. Thus, according to such judgements of the same parameters in "classical" coherence (Zwiener *et al.* 1991, 1995), we have determined these high-resolution coherence values < 0.40 as uncertain, changing between 0.40 and 0.95 as gradual, and > 0.95 as complete coordination.

Results

Original instantaneous heart rate, RESP, and noninvasively recorded BPF (Fig. 1) exhibited the well-known physiological fluctuations. The noninvasive arterial blood pressure recordings showed the same short-term pattern as in invasive blood pressure recordings (Imholz *et al.* 1988). The sequences of ordinary and partial coherence of high time resolution within the range of RESP frequencies always showed time-related patterns regarding their changing strength (Figs 2-4) which could not be correlated to any properties of the autonomous time series themselves.

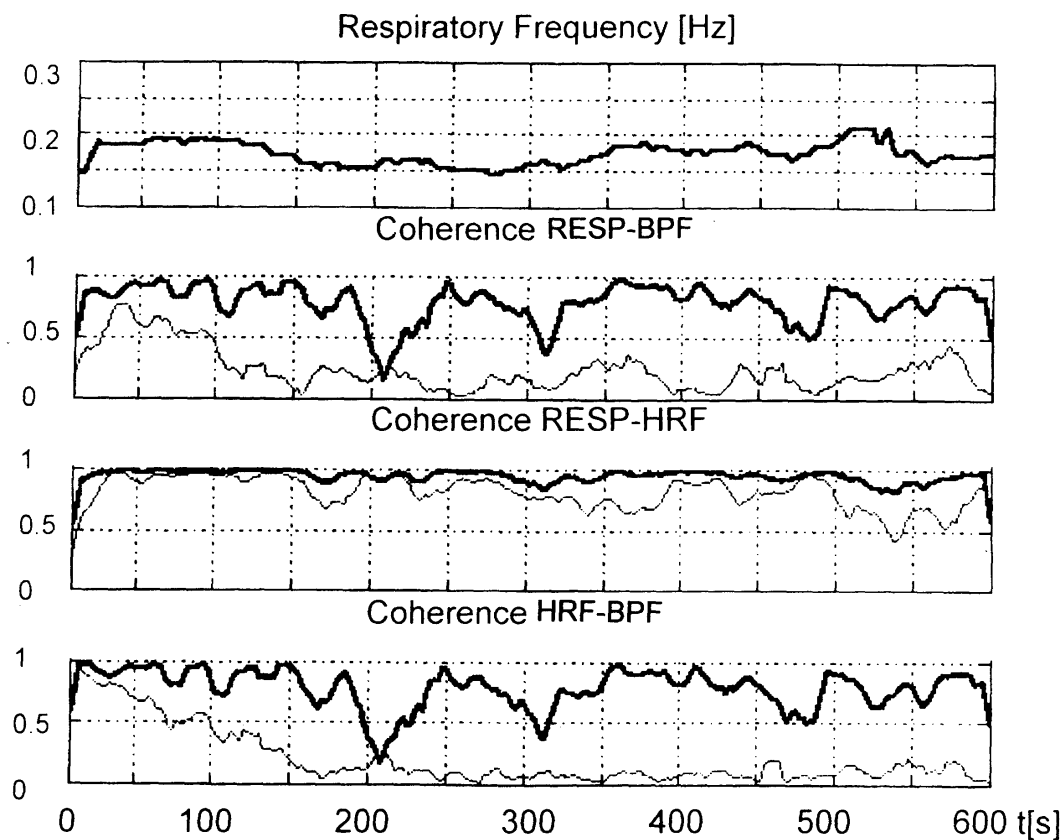


Fig. 2. Respiratory frequency, ordinary (bold lines) and partial short-term coherence (thin lines) between respiratory movements and arterial blood pressure fluctuations (RESP-BPF and RESP-BPF/HRF), respiratory movements and heart rate fluctuations (RESP-HRF and RESP-HRF/BPF), and heart rate fluctuations and arterial blood pressure fluctuations (HRF-BPF and HRF-BPF/RESP) from the recording of Figure 1 at rest (note continuous high, but slightly fluctuating RESP-HRF and more fluctuating RESP-HRF/BPF and almost from the initial 150 s lasting trends of the partial coherence of RESP-BPF/HRF and HRF-BPF/RESP in the same direction).

Table 1. Numbers of subjects showing dynamic patterns of partial (pa) and ordinary (or) coherence of high resolution between RESP and HRF, RESP and BPF, and between HRF and BPF during rest conditions and during paced breathing.

	RESP-HRF				RESP-BPF				HRF-BPF			
	rest		paced		rest		paced		rest		paced	
	pa	or	pa	or	pa	or	pa	or	pa	or	pa	or
<i>Short-term fluctuations</i>	4	6	3	4	4	5	4	3	1	3	2	2
<i>Short-term changes</i>	3	0	3	2	3	4	1	2	0	4	0	0
<i>Trends</i>	4	1	1	1	3	1	1	3	3	1	5	3
<i>Longer changes of the level</i>	3	1	1	1	1	2	1	3	1	2	0	3

$N = 6$; for definitions of patterns see the Results section.

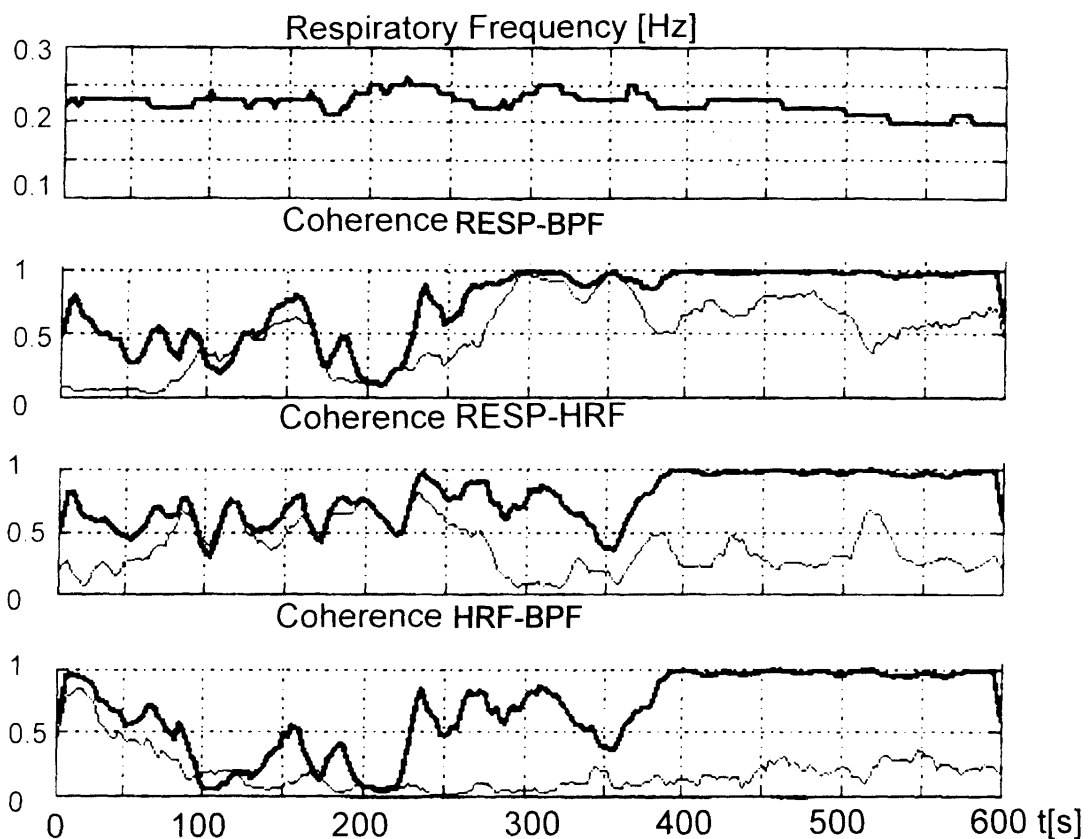


Fig. 3. The same respiratory and coherence parameters as in Figure 2 in a 27-year-old healthy male volunteer at rest (Note opposite behavior of RESP-BPF/HRF and RESP-HRF/BPF and time synchronous increase of RESP-BPF/HRF and decrease of RESP-HRF/BPF after 240 s and very similar RESP-HRF and HRF-BPF after 250 s).

Partial short-term coherence at rest

Partial coherence concerns the direct (linear) interactions between two time series and excludes the contribution of a third one. In more than half of subjects (4 out of 6), the sequences of partial coherence RESP-HRF/BPF moved mainly above 0.5 level (Fig. 2) and were frequently between 0.70 and 0.95 in intervals of 150-500 s. Thus, in partial coherence RESP-HRF/BPF, the intervals mainly changed between different gradual and seldom complete coordinations. Two subjects with different levels did not exhibit different heart rate or blood pressure levels or different autospectra of HRF or BPF. The partial coherence sequences RESP-BPF/HRF often had coherence values < 0.4 and partial HRF-BPF/RESP coherence sequences had values mainly < 0.4 (Figs 2 and 3), i.e. partial RESP-BPF/HRF coherence was often uncertain or absent, and HRF-BPF/RESP coherence had mainly rather absent coordinations. Otherwise, the RESP-BPF/HRF coherence sequences sometimes increased to 0.5-0.7 (Fig. 2, one subject) and up to 0.9 during 25-105 s (Fig. 3, five subjects), but never to 1.0. If

the coherence sequence of RESP-BPF/HRF was above 0.5 for longer time than 80 s (four subjects), then almost always the corresponding RESP-HRF/BPF coherence was below 0.5 (Fig. 3).

Concerning the dynamic patterns within these partial coherence sequences of high time resolution within the frequency band of RESP, there were often systematic patterns as short-term fluctuations (amplitudes > 0.5 , 25-60 s; Figs 3 and 4, Table 1), short-term changes (> 0.5 , 60-80 s, Figs 2 and 3), trends (> 0.5 , 80-210 s, Figs 2 and 3), and longer lasting changes in the level of coherence (> 0.5 , > 300 s, Fig. 3, Table 1). As shown in Table 1, partial RESP-HRF/BPF coherence included all forms of these patterns.

As far as the direction of trends and changes of these sequences of partial coherence are concerned, five subjects showed mainly or completely opposite changes between partial RESP-HRF/BPF and RESP-BPF/HRF coherence (Figs 3 and 4, after 250 s). A simultaneous increase of more than one partial coherence above 0.6 has never been observed.

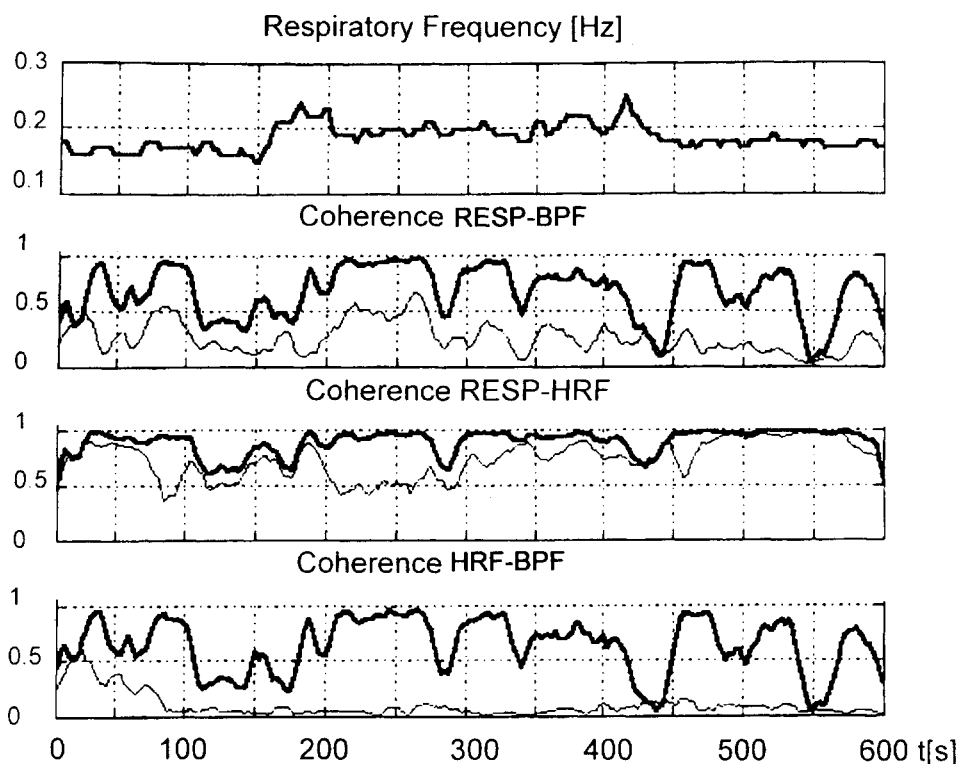


Fig. 4. The same respiratory and coherence parameters as in Figure 2 in a 34-year-old healthy male volunteer during paced respiration (pacing frequency 0.18 Hz according to the mean spontaneous respiratory frequency; see mainly low RESP-BPF/HRF, always low HRF-BPF/RESP, but always gradual up to complete RESP-BPF/HRF coherence).

Ordinary short-term coherence at rest

Ordinary coherence included all (linear) common dynamics of two time series, i.e. besides the direct interactions the same influences of other time series upon both investigated series are also included.

The ordinary coherence of RESP-BPF and HRF-BPF within the frequency range of RESP was almost always essentially higher than the corresponding partial one (Figs 2 and 3). The ordinary coherence showed a pattern in a similar time range as the partial one (Table 1, Figs 2 and 3), but in ordinary coherence of RESP-BPF and HRF-BPF the amplitudes of short-term fluctuations were often larger (up to 0.8, Figs 2 and 3). As is shown in Table 1, there exist all of the patterns of coherence changes as is described above in partial coherence with the exception of those of short-term changes of RESP-HRF and HRF-BPF coherence.

The two ordinary coherence sequences corresponding to the current smallest partial coherence values were almost always equal (Fig. 2, RESP-BPF and HRF-BPF; Fig. 3, RESP-HRF and HRF-BPF, after 280 s). In four cases, these were the ordinary RESP-BPF and HRF-BPF coherence. This mainly suggests a similar or an identical respiratory influence on both HRF and BPF, but to the latter indirectly, i.e. partly *via* HRF. If the partial coherence RESP-BPF/HRF was high, (Fig. 3, after 280 s), the remaining two ordinary coherence were identical or very similar. This means that the direct main coupling between RESP and HRF is transferred to that between RESP and BPF. Consequently, the high ordinary coherence RESP-HRF must be mediated indirectly (from RESP *via* BPF to HRF).

As far as the direction of change of trends or changes of levels of ordinary coherence sequences are concerned, the changes were almost always in the same direction (Figs 2 and 3), although with often smaller amplitudes in the ordinary RESP-HRF coherence.

Partial short-term coherence during paced respiration

During paced respiration, there were also considerable fluctuations of the sequences of partial RESP-HRF/BPF, RESP-BPF/HRF, and HRF-BPF/RESP coherence regarding their patterns and amplitudes (Fig. 4). Except one case, the partial RESP-HRF/BPF coherence was also strong (> 0.7). The partial coherence of RESP-BPF/HRF and HRF-BPF/RESP were mainly below 0.5, but in some parts (30-150 s) they were above 0.5. This was shorter than in the records when subjects

were at rest. Apart from the exception mentioned, the partial RESP-HRF/BPF coherence decreased below 0.5 during a very short time period (26-30 s). In all subjects, the partial HRF-BPF/RESP coherence was also very shortly above 0.5 (up to 30 s).

Concerning the dynamic patterns of these partial coherence sequences, they were the same as in rest, i.e. short-term fluctuations, short-term changes, trends, and longer lasting changes of the coherence level (Table 1). The only exception was the absence of short-term changes and longer lasting changes of the level in partial HRF-BPF/RESP coherence.

Regarding the direction of changes, it should be noted that the opposite changes occurred in three cases between partial coherence RESP-BPF/HRF and RESP-HRF/BF and in two cases between RESP-HRF/BPF and HRF-BPF/RESP regarding the direction of changes. Two concomitant partial coherences have never been above 0.6.

Ordinary short-term coherence during paced respiration

These ordinary RESP-HRF, RESP-BPF, and HRF-BPF coherences and their sequences also showed similar properties as those recorded at rest. During paced respiration, as in recordings at rest, the two ordinary coherences between these two parameters that had the lowest corresponding partial coherences were equal or almost equal (Fig. 4, RESP-BPF and HRF-BPF). The RESP-BPF and HRF-BPF short-term fluctuations were higher than those of the corresponding partial coherences (0.5-0.9). Apart from one exception of absent short-term changes of HRF-BPF coherence, there were also similar short-term fluctuations, changes, trends, and longer changes of the coherence level as in the dynamics of coherence at rest (Table 1).

Regarding the direction of changes in the sequences of ordinary coherence, there were mainly changes in the same direction between all pairs of ordinary coherence (Fig. 4).

Discussion

The analysis of partial and ordinary coherences of short-term resolution between RESP, HRF, and BPF of conscious humans rarely revealed constant high values in the sense of complete or absolute coordination (von Holst 1939, Barmer and Gebber 1976). Instead, changes between absolute, gradual or absent coherences were

mainly found here. These indicate relative or “sliding” coordinations (von Holst 1939, Koepchen *et al.* 1981) and their short-term dynamics. Coordinations between RESP and HRF, RESP and BPF, but seldom between HRF and BPF, including the patterns of changes, have also been verified by the calculation of partial coherence. It means that there are direct and changing coordinations between all three parameters within the respiratory frequency range, but to a different extent: Within the partial coherences, RESP-HRF/BPF ones are the strongest and most frequent coordinations (Fig. 2), the RESP-BPF/HRF coherences are mainly weaker and less frequently above 0.4 (Fig. 3), i.e. they are seldom at the levels defined as gradual or complete coherence. HRF-BPF/RESP coherence is the weakest and very rarely above 0.4.

The determined patterns of coherence sequences of high time resolution, such as short-term fluctuations, short-term changes, trends, and longer lasting changes of coherence levels are frequent changes between complete, gradual, and partly absent coordination within the same time series. Therefore, it is not possible to describe the real current coupling between RESP, HRF, and BPF by the “classical” coherence of Fast-Fourier-Transform. In cases of short-term changes between two coherence levels, as in Figure 3, we would often calculate a non-existing mean between two very different levels of coherence. Additionally, coherence calculation by this “classical” procedure (*via* Fast-Fourier-Transform) requires a stationary time series which is often not present in autonomous time series. Therefore, the use of methods for estimation of coherence of short-term resolution, such as this time-varying trivariate autoregression (Arnold *et al.* 1998), is essential for the calculation of short-term dynamics of coherence.

These strongly time-dependent short couplings, especially within the RESP/HRF coordination in the sense of respiratory sinus arrhythmia but also within the more seldom RESP/BPF couplings, have not been described yet. The complex mechanism of origin of the respiratory sinus arrhythmia (Richter and Spyer 1990, Berntson *et al.* 1993) does not allow a decisive explanation of the physiological background of the observed dynamics. However, certain provisional assignments to physiological mechanisms are possible. The main mechanisms of respiratory sinus arrhythmia are (i) the complex interaction of the respiratory rhythm

within the brainstem with its vagal cardiomotoric activity including nervous pulmonary feedbacks, (ii) hemodynamic effects of the mechanical RESP upon nerve-mediated heart reflexes, and (iii) the effect of intrathoracic pressure changes upon the sinoatrial node (for view see Richter and Spyer 1990, Berntson *et al.* 1993). Because of the controlled resting position and the regular breathing of all subjects, it is unlikely that such hemodynamic changes occur at such short intervals as are found for these rapidly changing coupling patterns. Thus, it is rather the changing degree of nervous coordination, which should cause the latter patterns.

In comparison with the RESP-HRF/BPF couplings quantified by their partial coherence, the RESP-BPF/HRF couplings quantified in the same way are usually weaker and less frequent. These are weaker and more seldom relative coordinations in the sense of von Holst (1939). Further studies, including repeated recordings in the same subject, could clarify whether individual properties are responsible for these differences.

The main mechanisms of BPF within the respiratory frequency in awake human beings as well as in other mammals (Richter *et al.* 1991) are (i) fluctuations of cardiac output within the respiratory rhythm mediated by the hemodynamic effects of mechanical breathing movements (Stauss *et al.* 1998) or by nerve-mediated contractility changes (Massari *et al.* 1998) and, perhaps, (ii) the effect of breathing-related fluctuations of vasomotor sympathetic activity (Croix *et al.* 1999). At least in humans and in rats, this latter mechanism is not certain because these frequencies of sympathetic activity could be filtered by the slow transmission at the neuroeffector junction (Persson *et al.* 1992, Stauss *et al.* 1995, 1998). Using the stimulation of skin sympathetic fibers *via* microneurography needles in healthy volunteers Stauss *et al.* (1998) have found low pass filter properties of sympathetic vascular transmission with a cut-off frequency above 0.1 Hz. However, Baron *et al.* (1996) showed that respiratory modulations of peripheral blood flow also occur in humans with a latency of 4.6 s, which were distinctly lower on the sympathectomized side. Thus, during slow respiration BPF can be influenced by sympathetic efferent activity synchronous with respiration. Feedbacks from pulmonary stretch receptors and baroreceptors are the dominant determinants of this respiratory modulation of sympathetic efferent activity in awake human beings (Croix *et al.* 1999).

A main mediation of respiratory BPF *via* physiological amounts of respiratory sinus arrhythmia is not very likely. After heart transplantation, Macor *et al.* (1994) have found that respiratory sinus arrhythmia is almost absent in patients, but respiratory BPF always remains unchanged.

When the partial coherence sequence of RESP-HRF/BPF decreases, the partial coherence sequence of RESP-BPF/HRF, i.e. that between RESP and BPF, increases in five cases. These opposite changes are often mirror images of each other (Fig. 3, second part). Thus, there is a reciprocal relationship between these two relative coordinations in four cases. Therefore, in conscious humans we can assume reciprocal changes in the influence of autonomic efferent activity between arterial blood pressure and heart rate control. This pattern suggests a competitive change of relative coordination between RESP/HRF and RESP/BPF, but not HRF/BPF. The reason for this can not be determined from our own results. However, the physiological explanation could be (i) the "spreading" or "contracting" of rhythms observed in the nervous control of the same autonomous parameters (Koepchen *et al.* 1981), and (ii) the mentioned "dissociation" between similar or same rhythms of efferent sympathetic and phrenic nerve discharges as has been shown in anesthetized cats (Barman and Gebber 1976).

In comparison with the short-term partial coherence sequence of RESP-HRF/BPF and RESP-BPF/HRF, that of HRF-BPF/RESP was always smaller and was seldom above 0.4. Thus, there was a weak or absent direct coordination between HRF and BPF within the respiratory frequency range. This result is not trivial because the common brainstem generator (Langhorst *et al.* 1983, Richter and Spyer 1990, Richter *et al.* 1991) can provide an efferent outflow that has the same frequency as the central respiratory oscillator, but is not mediated by it (Barman and Gebber 1976, Langhorst *et al.* 1983).

Compared with the partial coherence sequences, the corresponding ordinary sequences of RESP-BPF and HRF-BPF showed quite another picture because the ordinary coherence of RESP-BPF and HRF-BPF are always essentially higher than their partial coherence. They are even higher, if the partial coherence of RESP-BPF is very high. Therefore, the difference between the partial and ordinary coherence of RESP-BPF and HRF-BPF is very likely result of the simultaneous influence of efferent activities upon the BPF and HRF in

or close to the respiratory rhythm. This is not the result of a direct HRF-BPF interaction. In most cases, this influence is essentially lower on the BPF, but does often exist. Recently, Cohen *et al.* (1997) also described lower frequencies of sympathetic efferent activity in cats that vary in time between stronger, weaker and absent components showing a respiratory rhythm.

The changes of these three ordinary coherence sequences, almost always in the same direction, can be explained by the respiratory or respiratory-like rhythm as the main influence upon HRF and BPF. This is supported by the often opposite direction of the corresponding partial coherences, but the same direction of the ordinary ones. This demonstrates that a greater part of the "whole", i.e. the ordinary coherence, comes from respiratory or respiratory-like rhythm, the contribution of which varies with time.

Similar or identical results obtained during paced respiration suggest that voluntary impulses influencing the respiratory rhythm do not obviously change these short-term couplings between RESP, BPF, and HRF in comparison with those during the resting state. It has already been reported by Madden and Savard (1995) that conscious control of breathing exerts no influence upon HRF and systolic blood pressure variability in healthy men and women. We can therefore assume (i) that the dynamics of relative coordination during physical rest do not depend essentially on voluntary impulses regulating respiration, and (ii) that these dynamics are rather the result of changing functional organization of brainstem neuronal networks related to respiratory and cardiovascular control and their effects as described by Langhorst *et al.* (1983) and Gebber *et al.* (1994a,b).

We can only determine linear coordination or couplings by the method used here. However, a complete determination of all the relations requires nonlinear methods to be employed. We have recently determined (Hoyer *et al.* 1997, 1998) nonlinear components between cardiorespiratory interactions showing nonlinear and relative coordinations which also vary.

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References

- ARNOLD M, MILTNER W, WITTE H, BAUER R, BRAUN CH: Adaptive AR modeling of nonstationarity time series by means of Kalman filtering. *IEEE Trans Biomed Eng* **45**: 553-562, 1998.
- ARNOLD M, WITTE H, MILTNER W, SCHELENZ CH: Time variant analysis of coherence and quadratic phase coupling in brain electrical processes. *Med Biol Eng Comput* **37** (Suppl 2): 424-425, 1999.
- BARMAN SM, GEBBER GL: Basis for synchronization of sympathetic and phrenic nerve discharge. *Am J Physiol* **231**: 1601-1607, 1976.
- BARON R, HÄBLER HJ, HECKMANN, PARSCHE H: Respiratory modulation of blood flow in normal and sympathectomized skin in humans. *J Auton Nerv Syst* **60**: 147-153, 1996.
- BENDAT IS, PIERSOL AG: *Random Data Analysis and Measurement Analysis Procedures*. John Wiley, New York, 1986.
- BERNTSON GG, CACIOPPO JT, QUIGLEY KS: Respiratory sinus arrhythmia: Autonomic origins, physiological mechanisms, and psychophysiological implications. *Psychophysiology* **30**: 183-186, 1993.
- GASTIGLIONI P, PEDOTTI A, DI RIENZO M: An algorithm for tracking the effects of respiration on blood pressure and heart rate in unrestrained animals. In: *Blood Pressure and Heart Rate Variability*. M DI RIENZO, G MANCIA, G PARATI, A PEDOTTI, A ZANCHETTI (eds), IOS Press, Amsterdam, 1992, pp 75-84.
- CHEN HH, GUO L: *Identification of Stochastic Adaptive Control*. Birkhäuser, Boston, 1991.
- COHEN MI, YU QP, HUANG WX: Fast (3 Hz, 10 Hz) and slow (respiratory-related) rhythms in sympathetic nerve and unit discharges of cat. *Proc XXXIII Congr IUPS*, St. Petersburg, P 061.30, 1997.
- CROIX CMS, SATOH M, MORGAN BJ, SKATRUD JB, DEMPSEY, JA: Role of respiratory motor output in within-breath modulation of muscle sympathetic nerve activity in humans. *Circ Res* **85**: 457-469, 1999.
- FIŠER B, HONZÍKOVÁ N, PEŇÁZ J: Power spectra of spontaneous variations of indirectly recorded blood pressure, heart rate, and acral flow. *Automedica* **2**: 143-147, 1978
- GEBBER GL, ZHONG S, BARMAN SM, PAITEL Y, ORER HS: Differential relationship among the 10-Hz rhythmic discharges of sympathetic nerves with different targets. *Am J Physiol* **267**: R387-R399, 1994a.
- GEBBER GL, ZHONG S, BARMAN SM, ORER HS: Coordination of the cardiac-related discharges of sympathetic nerves with different targets. *Am J Physiol* **267**: R400-R407, 1994b.
- HOYER D, HADER O, ZWIENER U: Relative and intermittent cardiorespiratory coordinations. *IEEE Eng Med Biol Mag* **16**: 97-104, 1997.
- HOYER D, BAUER R, WALTER B, ZWIENER U: Estimation of nonlinear couplings on the basis of complexity and predictability – a new method applied to cardiorespiratory coordination. *IEEE Trans Biomed Eng* **45**: 545-552, 1998.
- IMHOLZ BPM, VAN MONTFRANS GA, SETTELS JJ, VAN DER HOEVEN GM, A KAREMAKER JM, WIELING W: Continuous non-invasive pressure monitoring: reliability of Finapres device during the Valsalva manoeuvre. *Cardiovasc Res* **22**: 390-397, 1988.
- KOEPCHEN HP, KLÜSSENDORF D, SOMMER D: Neurophysiological background of central neural cardiovascular-respiratory coordination: basic remarks and experimental approach. *J. Auton Nerv Syst* **3**: 335-368, 1981.
- KORNMÜLLER H: *Digitale Signalverarbeitung*. Springer, Berlin, 1991.
- LANGHORST P, SCHULZ B, SCHULZ G, LAMBERTZ M: Reticular formation of the lower brain stem. A common system for cardiorespiratory and somatomotor functions. Discharge patterns of neighbouring neurons influenced by cardiorespiratory and respiratory afferents. *J Auton Nerv Syst* **9**: 411-432, 1983.
- MACOR F, FAGARD R, VAN HAECKE J, AMERY A: Respiratory-related blood pressure variability in patients after heart transplantation. *J Appl Physiol* **76**: 1961-1962, 1994.
- MADDEN K, SAVARD GK: Effects of mental state on heart rate and blood pressure variability in men and women. *Clin Physiol* **15**: 557-569, 1995.
- MASSARI VJ, DICKERSON LW, GRAY AL, LAUENSTEIN JM, BLINDER KJ, NEWSCOME JT, RODAK DJ, FLEMING TJ, GATTI RJ, GILLIS RA: Neural control of left ventricular contractility in the dog heart:

- synaptic interactions of negative inotrope vagal preganglionic neurons in the nucleus ambiguus with tyrosine hydroxylase immunoreactive terminals. *Brain Res* **802**: 205-220, 1998.
- MOLHOEK GP, WESSELING KH, SETTELS JJ: Evaluation of the Peñáz servo-plethysmo-manometer for the continuous, non-invasive measurement conditions and factors affecting reliability. *Basic Res Cardiol* **79**: 598-609, 1984
- PEÑÁZ J: Photoelectric measurement of blood pressure, volume, and flow in the finger. *Digest 10th Int Conf Med Biol Eng*, Dresden 1973, p 104.
- PERSSON PB, STAUSS H, CHUNG O, WITTMANN U, UNGER T: Spectrum analysis of sympathetic nerve activity and blood pressure in conscious rats. *Am J Physiol* **263**: H1348-H1355, 1992.
- RICHTER DW, SPYER KM Cardiorespiratory control. In: *Central Regulation of Autonomic Functions*. AD LOEWY, KM SPYER (eds), Oxford University Press, New York, 1990, pp 189-207.
- RICHTER DW, SPYER KM, GIBEY MP, LAWSON EE, BAIN TOWN CR, WILHELM Z: (1991) On the existence of a common cardiorespiratory network. In: *Cardiorespiratory and Motor Coordination*. HP KOEPCHEN, T HUOPANIEMI (eds), Springer, Berlin, 1991, pp 118-130.
- STAUSS HM, RETTIG R, PERSSON PB, UNGER T: Does low frequency power of arterial blood pressure reflect sympathetic tone? *J Auton Nerv Syst* **54**: 145-154, 1995.
- STAUSS HM, ANDERSON EA, HAYNESS WG, KREGEL KC: Frequency response characteristics of sympathetically mediated vasomotor waves in humans. *Am J Physiol* **274**: H1277-H1283, 1998.
- VON HOLST E: Die relative Koordination als Phänomen und als Methode zentralnervöser Funktionsanalyse. *Ergebn Physiol* **42**: 228-306, 1939.
- ZWIENER U, BAUER R, ROTHER M, SCHWARZ G, WITTE H, LITSCHER G, WOHLFAHRT M: Disturbed brain stem interaction and forebrain influences within cardiorespiratory coordination - experimental and clinical results. In: *Cardiorespiratory and Motor Coordination*. HP KOEPCHEN, T HUOPANIEMI (eds), Springer-, Berlin, 1991, pp 85-96.
- ZWIENER U, LÜTHKE B, BAUER R, HOYER D, RICHTER A, WAGNER H: Heart rate fluctuations of lower frequencies than respiratory rhythm but caused by it. *Pflügers Arch* **429**: 455-461, 1995.
- ZWIENER U, BAUER R, HOYER D, LÜTHKE B, WALTER B, SCHMIDT K, HALLMEYER S, KRATZSCH B, EISELT M: Deterministic-chaotic and periodic properties of heart rate and arterial pressure fluctuations and their mediation in piglets. *Cardiovasc Res* **31**: 455-465, 1996a.
- ZWIENER U, HOYER D, LÜTHKE B, SCHMIDT K, BAUER R: Relations between parameters of spectral power densities and deterministic chaos of heart-rate variability. *J Auton Nerv Syst* **57**: 132-135, 1996b.

Reprint requests

Prof. Dr. Dr. Ulrich Zwiener, Institut für Pathophysiologie, Klinikum der Friedrich-Schiller-Universität, Nonnenplan 2, D-07740 Jena, Germany, tel: 0049-3641-938950, fax: 0049-3641-938952, e-mail: uzwi@mti-n.uni-jena.de