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Phase- and Frequency Coordination of Cardiac and Respiratory Function

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ABSTRACT

ECG and respiration (by nose thermistor sensor) were measured in 160 healthy volunteers under resting conditions. Frequency analysis allowed to distinguish fast (center frequency ≈ 0,25 Hertz), medium (center frequency ≈ 0,1 Hertz) and slow waves (center frequency ≈ 0,05 Hertz) of heart rate variability. The fast waves are related to respiratory sinus arrhythmia, which mirrors parasympathetic tone and the slow waves are mainly connected with the sympathetic nervous activities, whereas medium waves are influenced by both the sympathetic and the parasympathetic nervous system.

Simultaneously we calculated the heart – respiration coupling by recording a total of ≈ 18.000 respiratory cycles as well as the time from the R-peak to the onset of the next inspiration. Three distinct peaks of coincidence are related to afferents discharging in the isometric systolic phase (peak 1), to the baroreceptor afferents in the great arterial vessels (peak 2) and afferents excited in the relaxation or diastolic filling phase (peak 3), respectively .

The pulse-respiration quotient (PRQ) represents the state of the autonomic nervous system (ANS): Ergotropic conditions lead to an individual´s PRQ with no special preference, whereas during trophotropic conditions the PRQs exhibit a preference for a 4:1 ratio. The latter is shown by measurement under resting conditions.

The above-mentioned cardio-respiratory interactions could be used for a multidimensional assessment of autonomic functions. Differentiation between ergotropy and trophotropy, sympathetic or parasympathetic arousal, sympathicotony and parasympathicotony is possible using these parameters and allows to study the autonomic activity from different viewpoints. Moreover, such a multidimensional description of the ANS might prove to be a valuable instrument for the clinical investigation of the state of the autonomic nervous system.

Abstracting keywords: Heart rate variability, respiratory sinus arrhythmia, pulse-respiration coupling, pulse-respiration quotient, autonomic nervous system.

1. INTRODUCTION

The function of the autonomic nervous system (ANS) in the body is based on two seemingly divergent principles: on one hand homoiostasis, maintained by hu-

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moral as well as autonomic control loops (e.g. in thermoregulation or blood pressure control), assures equilibrium in a changing environment.

On the other hand, endogenous rhythms fit the organism's physiological functions into the pattern of geological rhythms like the day-night cycle or the seasons of the year. As an example, the body "waits" every morning for light to trigger the circadian phase of the autonomic system (1). Coordination between biological rhythms is also maintained, especially during periods of rest. This is obviously needed to optimize interaction among body functions and is most prominent in cardiorespiratory rhythms.

As a third task, the dynamic regulation of physiological variables answers demands imposed by everyday tasks like postural changes, different activity levels etc.

Looking at the whole spectrum of biological rhythms (2, 3, 4) it becomes obvious that all parameters that vary with time should be included in order to obtain a better understanding of biological rhythms and hence chronobiology. The time-spectrum of biological functions in the organism has respiration and heart rhythm at its center. Except the sleep-wake-cycle and the menstruation rhythm, these two rhythms are the only biological cycles everyone experiences. The heart rate (HR), which is not under conscious control, reflects a multitude of autonomic cycles (5). Among these the respiratory cycle (2-7 sec range), blood pressure rhythms (10 sec range) and peripheral blood flow variations (1 min range) are the most prominent.

The analysis of heart rate reveals a definite connection between the fast variations of heart rate variability (HRV) and vagal parasympathetic arousal (5, 6). Parasympathetic tone has been shown to be directly related to the amount of rapid HRV (7, 8) reflecting respiratory changes in the cardiac rhythm.

Raschke et al. (9) and Engel et al. (10) have investigated in detail the coupling between inspiration and the cardiac cycle. Few investigations have yet been undertaken to use this information as a diagnostic tool (11, 12).

Hildebrandt et al. (3, 13) and Raschke (9) have shown the importance of the pulse-respiration quotient (PRQ) as an indicator of autonomic states: During the day, divergent PRQs in the range of 2:1 to 15:1 can be observed, whereas during sleep the PRQ approaches a 4:1 ratio in healthy subjects.

Coordination and coupling of the cardiorespiratory rhythms are obviously mediated by the ANS. Measurement of this phenomenon should give insight into ANS function or dysfunction.

This paper surveys the coupling and coordination in the cardiorespiratory system and relates them to the ANS state.

2. METHODS

ECG and respiration were measured in 160 healthy volunteers during 5 minutes of steady-state rest. For respiration, a nose-thermistor sensor as described by Raschke, 1981 (9), was used. This method was found to be most suitable for recording the onset of inspiration, due to its high sensitivity and very short time delay of the sensor. All physiological data were sampled at 200 Hertz and 10 bit resolution by a small data acquisition computer (14). R-R intervals were determined from the ECG with a digital matched filter which allows the recognition of the R-peak to 1 msec. The onset of inspiration was determined by a computer program to 5 msec. The distance between R-peak and inspiration onset was calculated from the respective signals to 5 msec and histograms were drawn with classes of 50 msec beginning with the preceding R-peak.

2.1. Frequency analysis of heart rate variability (HRV)

The raw HRV data of each person were analysed by a program developed in Matlab (Mathworks Comp.). Interbeat intervals more than 20% different from the previous RR intervals were eliminated by local interpolation and a maximum entropy Fourier transform was performed with the whole 5 min data sequence. The resulting smooth spectral estimation was plotted (Fig. 1). To obtain a time varying HRV signal, the different frequency peaks visible in the spectrum were filtered from the same data sequence. Three narrow-band digital filters using center frequencies of 0.25 Hertz, 0.1 Hertz and 0.05 Hertz were applied to the HRV data and the resulting fast, medium and slow waves were plotted vs. time. This display permits continuous observation of each of the 3 frequency bands present in the heart rate.

In the following, the different cardiorespiratory interactions are compiled for a multidimensional description of the autonomic nervous functional state.

3. RESULTS AND DISCUSSION

3.1. HRV

As mentioned above, HR is sensitive to many other physiological rhythms and factors: Inspiration and expiration, blood pressure rhythms, variations in peripheral blood flow, possibly thermoregulation (15), as well as excitement and exercise, all of which influence the interbeat interval and hence the HR (16). All these influences have their individual time characteristics. Frequency analysis of the HRV therefore makes it possible to distinguish among the different systems involved.

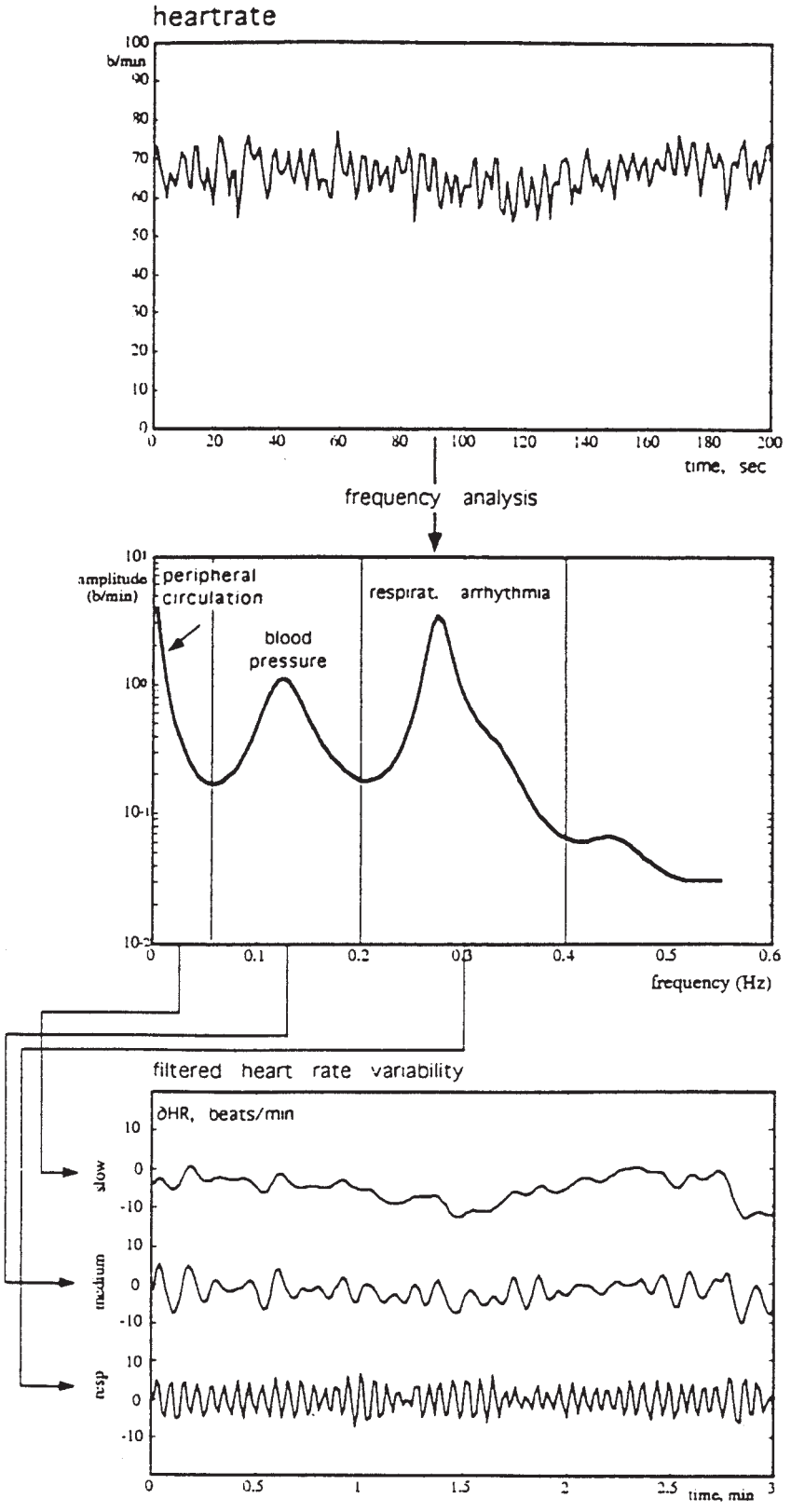
heartrate
b/min
time, sec
frequency analysis
amplitude (b/min)
peripheral circulation
blood pressure
respirat.
arrhythmia
frequency (Hz)
filtered heart rate variability
∂HR, beats/min
slow
medium
resp
time, min

Fig. 1 shows an example of two different ways to investigate HRV in the frequency or time domain. In the upper part of the figure, an original heart rate sequence lasting 200 seconds is shown. The trace is taken from a resting male healthy person, 25 years old, in supine position.

It can be seen that a fast variability corresponding to the respiratory rhythm is most prominent in the HRV. This phenomenon is well known as the respiratory sinus arrhythmia (RSA) and can also be seen in the frequency domain as a distinct peak around a center frequency of an approximate 0.25 Hertz (Fig. 1, middle part). Frequency analysis also reveals that two other peaks rise above the level of random variations: The 0.1 Hertz peak originating from blood pressure variations as well as the low frequency peak around 0.05 Hertz related to oscillations in peripheral blood flow.

Although frequency analysis impressively distinguishes the frequencies modulating HRV, the time information is lost due to the integrating properties of the maximum entropy Fourier transform used (Fig. 1 middle panel). To circumvent this problem, we tried a second approach and applied to the same data sequence a narrow band filtering algorithm with 3 different center frequencies. The bottom picture of Fig. 1 shows the resulting filtered time series: slow, medium and fast HRV waves can easily be distinguished and studied as they change over the 200 seconds. Elaborate investigations in the past have shown that the fast variations are a semiquantitative measure of parasympathetic vagal tone (7, 8, 17), the medium variation waves are influenced by parasympathetic as well as sympathetic arousal (18), whereas the slow waves are mainly connected to sympathetic nervous system rhythms (5, 6, 19). Integration of each of the waves therefore allows quantification of the peripheral tone of the respective major division of the ANS (6).

3.2. Pulse-respiration coupling

Galli discovered in 1924 (cit. in 9) that inspiration in humans does not start randomly during the cardiac cycle; actually, there are different time periods between two R-peaks of the ECG during which inspiration becomes more likely and occurs more often than during others, if a larger sample of inspirations is investigated. This coupling of inspiration to cardiac events underwent further study (20, 21, 22, 10, 23). Raschke in particular (9) performed extensive human studies and described the exact conditions determining the timing of inspiration with respect to heart beat.

Fig. 1. Heart rate variability.
a.) original data of heart rate (upper panel).
b.) spectral analysis of a.) showing at least 3 distinct peaks in the frequency domain (middle panel)
c.) band-filtering of a.) results in 3 different bands corresponding to respiration, blood pressure rhythms and variations coming from the peripheral circulation. (lower panel)

Fig. 2 shows an example of pulse respiration coupling in a healthy volunteer: Each inspiration during 5 minutes of quiet respiration is drawn in relation to the previous R-peak. It can be seen that the onset of inspiration (middle part of Fig. 2) is not evenly distributed along the cardiac cycle but takes place mainly during three distinct time intervals, which are graphically presented as peaks in the histogram (lower part of Fig. 2).

Since different individuals showed a variety of patterns, we tried to obtain an average histogram of inspiration onsets. For this purpose, ≈18000 inspirations of 160 persons were recorded, and the time from the preceding R-peak to the onset of inspiration was measured for each inspiration (Fig. 3). Three peaks in the histogram show that the prevailing intervals between heart beat and onset of inspiration are 50 - 150 msec (coupling peak 1, P1), 200 - 350 msec (P2) and 450 - 650 msec (P3), respectively. The first peak following immediately after the R peak clearly corresponds to the systolic contraction of the heart. Stretch receptors in the myocardium obviously elicit an impulse stream along autonomic afferents from the heart to the medullar centers, where activation of efferent respiratory neurons results in the onset of inspiration. During diastole, the histogram shows a further peak (P3). This peak may originate either from afferents activated by the myocardial endsystolic relaxation or from right atrial volume receptors streched by venous blood returning from the body. The remaining peak (P2) may be connected with the pulse wave passing by the baroreceptors in the carotid sinus (21, 22). Pulsesynchronous modulation of the afferent baroreceptor nerves was observed in single-cell preparations in cats (24).

3.3. Pulse-respiration quotient

In a multitude of studies, the Hildebrandt group (1) investigated the quotient of the frequencies of heart beat and respiration. It turned out that the PRQ shows inter-individual differences and variations during the 24 hour period. After several hours of sleep, the inter-individual differences are diminished and different groups of persons all develop a P/R ratio close to 4:1. In the morning, the individual PRQ, which can be below or above 4:1, reestablishes itself until the next night (3). It was shown in several investigations that ergotropic conditions lead to an individual PRQ with no special preference, whereas trophotropic conditions tend towards a general value of PRQ with a preference for a 4:1 ratio (25).

Fig. 4 shows the continuous pulse-respiration-quotient in 3 subjects in supine position over a period of 30 minutes. It can be observed, that periods of strong coordination (26) (straight horizontal shapes), periods of socalled 'weak coordination' (shifting lines) and chaotic episodes alternate within the figure. Deep inspiration (i) and breath holding or deep expiration (e) may trigger a change in PRQ (e.g. in Fig. 4c - increase of PRQ after deep inspiration: i). Whole number ratios (3:1, 4:1, 5:1) seem to be preferred by the human organism (3). Strong as

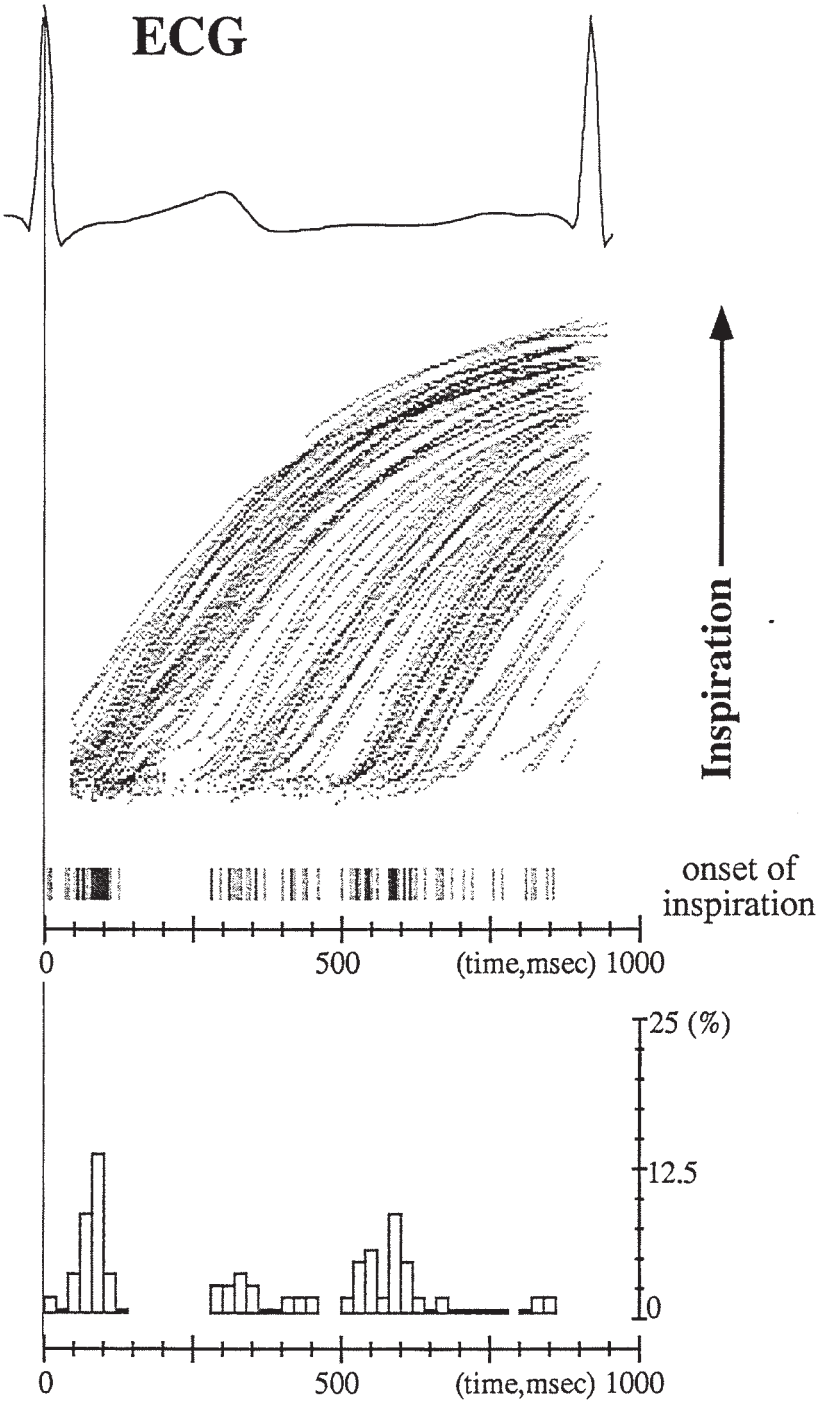

Fig. 2. PR coupling in one subject: Each inspiration during 10 minutes of quiet respiration is drawn as dotted line. Inspiration onsets are marked as solid lines at the bottom. Below the original data (middle panel) a histogram of the inspiration onsets is shown. It can be seen that inspirations are not evenly distributed during the cardiac cycle in this subject. There are 3 peaks and also periods where no inspirations occur.

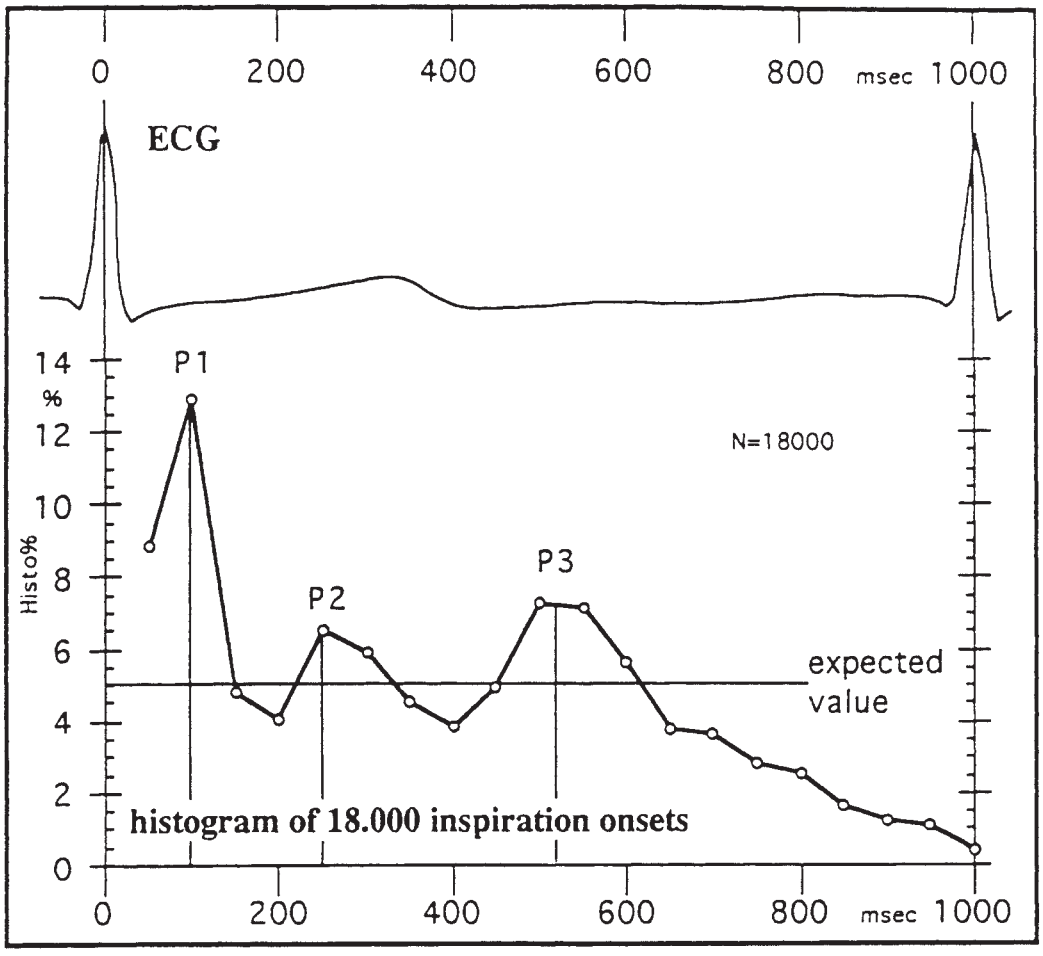

Fig. 3. PR Coupling in 160 healthy volunteers: the histogram shows the onset of ≈18.000 inspirations during quiet respiration distributed over the cardiac cycle. 3 distinct peaks can be observed, one during cardiac systole (P1), one during cardiac diastole (P3) and one in between (P2).

well as weak coupling may initiate whole number ratios. This can also be seen in a histogram of the pulse-respiration quotients observed in the same 160 resting healthy persons as in Fig. 3 (Fig. 5).

4. CONCLUSION

Cardiorespiratory rhythms are strongly modulated and coordinated by ANS functions. The periodicities of heart rhythm (ca 1 per sec) and respiration (ca 1/4 per sec) are suited to trace the varying time behaviour of the ANS with a resolution of 0.5 to 0.1 Hz. Within a few minutes, sufficient data can be obtained to characterize the actual ANS state in different dimensions. Circulation is central to the

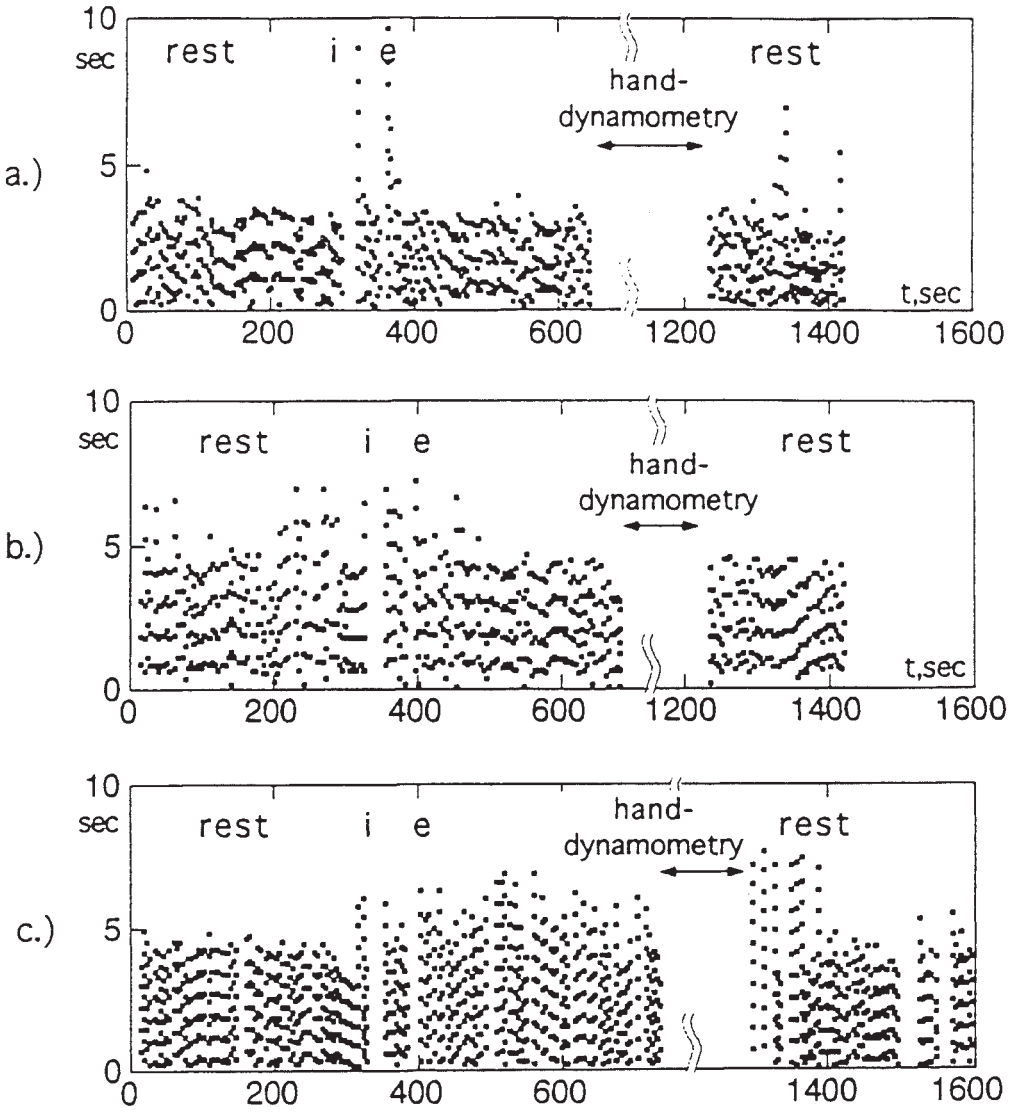

Fig. 4 a-c: Pulse-respiration quotient (PRQ):
The continuous relation between pulse and respiration is shown in 3 examples: Along the ordinate, time since last inspiration is shown. Each dot represents an R-peak of the ECG related to the previous inspiration (= zero on the ordinate).
A distinct pattern results.
The count of bands gives the instantaneous PRQ:
a: PRQ = 3:1
b: PRQ = 4:1
c: PRQ = 6:1 -9:1
No measurements of respiration were done during dynamometry.
i,e means deep inspiration rsp. expiration.

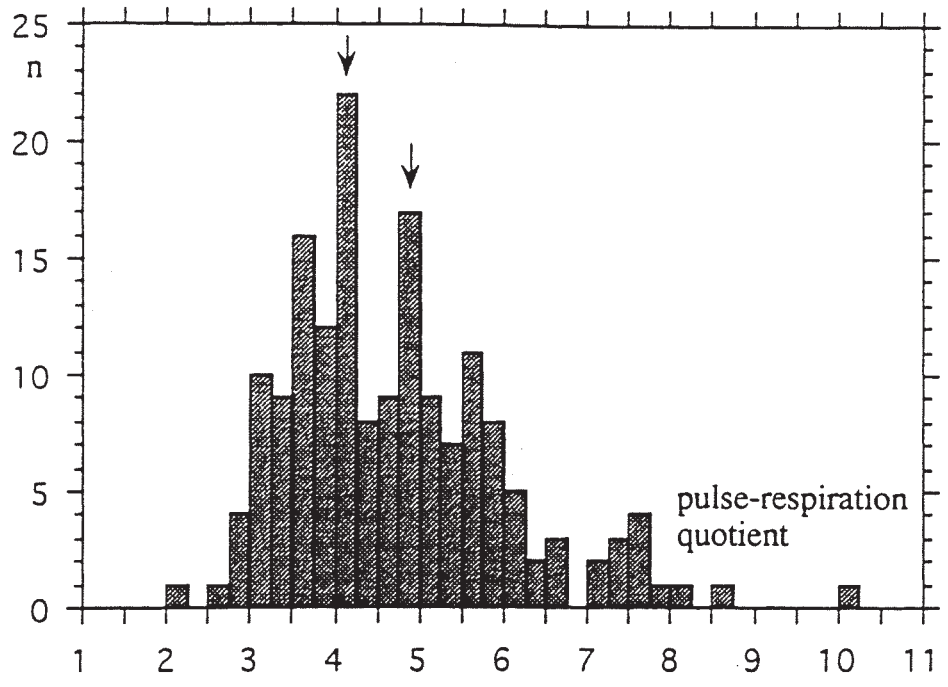

Fig. 5. Histogram of pulse-respiration quotients in 160 resting persons. The modulus of the histogram can be found at a PRQ of 4:1. Note that the histogram shows accumulations around whole- number ratios (4:1, 5:1) (arrows).

organism and is connected with and influenced by the total organismic situation. This might be the reason why Chinese doctors have chosen observation of the pulse as their main diagnostic tool as early as 2000 B.C.(27). The cardiac cycle promises surprisingly detailed and yet integral information not reflected in any other body function.

The three interactions described in this paper between respiration and circulation point to the coordinative function of the ANS. Some of the parameters are quantitative measures like RSA; others permit a more differentiated qualitative determination of the autonomic state. Taking several parameters together, the state of the autonomic nervous system may be described in a more appropriate way than using only single indicators. Dimensions like ergotropy and trophotropy, sympathetic or parasympathetic arousal, sympathicotony and parasympathicotony can be differentiated and studied in their time course. A multidimensional description of the ANS could prove to be a valuable instrument for the assessment of autonomic dysfunction.

Although only peripheral autonomic activity is measured, central events influence this activity and can be observed in the coordination of physiological parameters. In a future study, these parameters will be systematically investigat-

ed in a larger group of subjects and patients. A possible application of the methods in psychiatic research is described by Lehofer et al (28).

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