

# 534. Relation in-between autonomic cardiovascular control and central nervous system activity during sleep using spectrum-weighted frequencies

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(Received 30 November 2009; accepted 03 February 2010)

**Abstract.** The present study is concerned with relevance of the spectrum-weighted frequencies of both heart rate variability (HRV) and electroencephalogram (EEG). The frequencies represent the balance point of power within a certain spectral range. The predictive value of the frequencies and their mutual interrelations are demonstrated with respect to different sleep stages based on data from a single case. In particular, the revealed stage-dependent relationships between frequencies from HRV and EEG suggest a close interrelation between autonomic cardiovascular control and activity of central nervous system. The results demonstrate that the easy-to-assess frequencies may provide a simple indicator of the sleep quality within the scope of comfortable patient monitoring.

**Keywords:** autonomic cardiovascular control, central nervous system, spectrum-weighted frequencies.

## Introduction

Body activities are quantitatively assessed by the use of physiological indicators as blood pressure, temperature, and heart rate, the latter being derived from electrocardiography (ECG). Here the use of cardiorespiratory oscillations is of high importance, e.g., by monitoring heart rate variability (HRV) which reflects autonomic control of heart rate in a sophisticated way [1-3]. That is, HRV corresponds to activities of both body and central nervous system [1, 4]. On the other hand, mental activities, or generally speaking, activities of central nervous system, are registered by the use of electroencephalography (EEG). A special case of mental activity is given during sleep, which monitoring leads to sleep staging according to Rechtschaffen and Kales [5], and thus to a quantitative assessment of sleep efficiency. Usually investigation of sleep involves polysomnography (PSG) as the golden standard, requiring a high effort in both applied devices and attending (and scoring) physicians.

It should be noted that during human functioning a close relation between autonomic control of heart rate (reflected by HRV) and central nervous system (ECG) exists, especially during sleep when ambient factors do not have a prevailing influence. Therefore HRV might be used as a reflection of brain functions during sleep [6-8].

Obviously a low effort assessment of the body and mental activity is of high interest, combined with a minimal disturbance of the patient. Usually a high number of derived signals and elaborate signal processing methods are necessary to judge both activities, in particular during sleep [9, 10]. Thus, there is a need for more simple approaches. For instance, the authors in [11] have suggested the use of spectrum-weighted frequency  $f_w$  of EEG as an indicator of mental activity by utilizing shifts of  $f_w$ .

The rationale of the present study was to investigate the basic behaviour of  $f_w$  derived from HRV and EEG during sleep. In addition, possible mutual relations of  $f_w$  are investigated. Especially, established spectral ranges of HRV and EEG (Table 1) are taken into consideration in combination with separately considered sleep stages: awake before sleep (AW), rapid eye movements (REM), and drowsy to deep sleep stages (S1-S4).

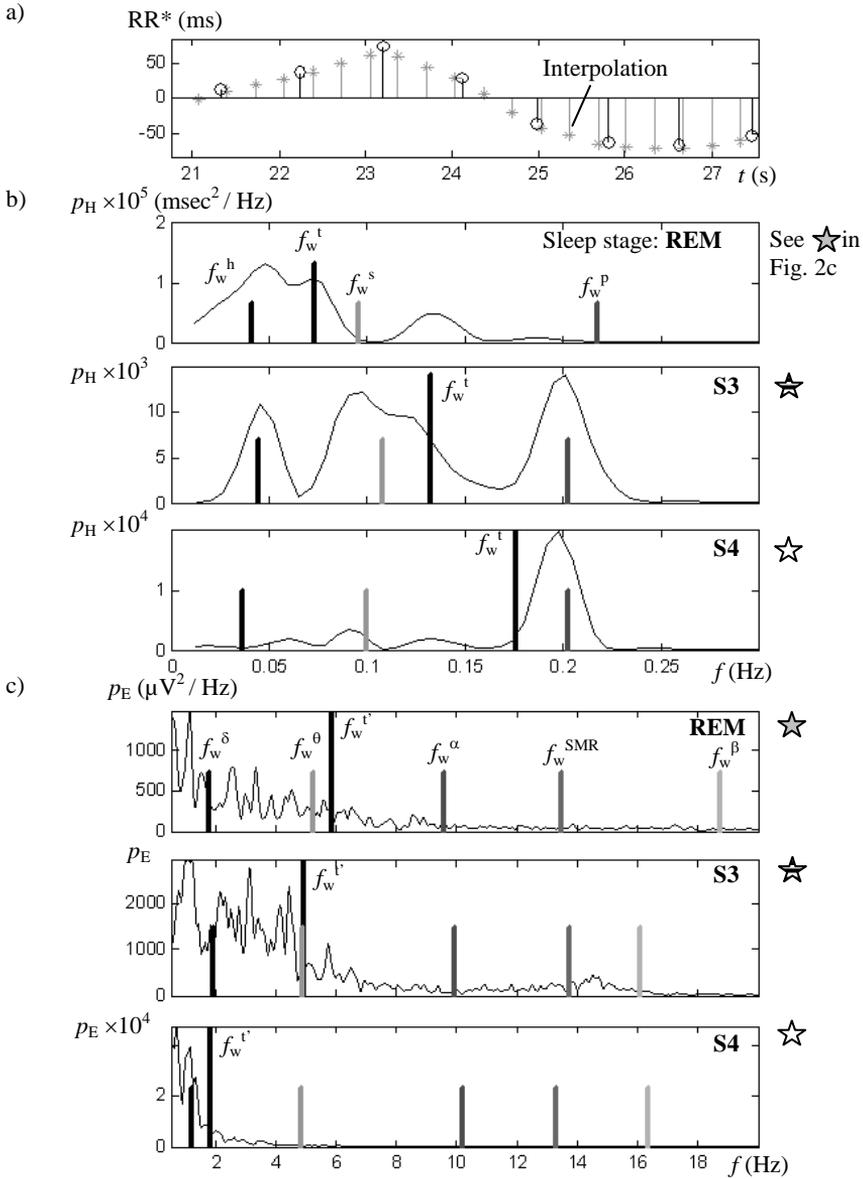
**Table 1.** Absolute mean values of spectrum-weighted mean frequencies  $f_w$  from HRV and EEG for different sleep stages and all night.

| Sleep stages/<br>total duration (min) | $f_w$ from HRV (Hz)          |                                  |                                     |  |                             |                                  |
|---------------------------------------|------------------------------|----------------------------------|-------------------------------------|--|-----------------------------|----------------------------------|
|                                       | Spectral ranges:             |                                  |                                     |  |                             |                                  |
|                                       | Total $f_w^t$<br>0.01-0.5 Hz | Humoral $f_w^h$<br>0.01-0.06 Hz  | Sympathetic $f_w^s$<br>0.06-0.15 Hz | Parasympathetic $f_w^p$<br>0.15-0.4 Hz |                             |                                  |
| Awake / 9                             | 0.076                        | 0.03                             | 0.101                               | 0.195                                  |                             |                                  |
| REM / 74                              | 0.076                        | 0.03                             | 0.092                               | 0.208                                  |                             |                                  |
| S1 / 0                                | -                            | -                                | -                                   | -                                      |                             |                                  |
| S2 / 88                               | 0.116                        | 0.03                             | 0.092                               | 0.194                                  |                             |                                  |
| S3 / 32                               | 0.128                        | 0.03                             | 0.092                               | 0.201                                  |                             |                                  |
| S4 / 22                               | 0.132                        | 0.03                             | 0.098                               | 0.203                                  |                             |                                  |
| All night 225                         | 0.104                        | 0.032                            | 0.093                               | 0.201                                  |                             |                                  |
| Sleep stages/<br>total duration (min) | $f_w$ from EEG (Hz)          |                                  |                                     |  |                             |                                  |
|                                       | Spectral ranges:             |                                  |                                     |  |                             |                                  |
|                                       | Total $f_w^t$<br>0.5-30.5 Hz | Delta $f_w^\delta$<br>0.5-3.5 Hz | Theta $f_w^\theta$<br>3.5-7.5 Hz    | Alpha $f_w^\alpha$<br>7.5-12.5 Hz      | SMR $f_w^{SMR}$<br>12-15 Hz | Beta $f_w^\beta$<br>12.5-30.5 Hz |
| Awake / 9                             | 6.85                         | 1.39                             | 5.13                                | 10.15                                  | 13.37                       | 20.43                            |
| REM / 74                              | 5.34                         | 1.61                             | 5.09                                | 9.54                                   | 13.48                       | 19.03                            |
| S1 / 0                                | -                            | -                                | -                                   | -                                      | -                           | -                                |
| S2 / 88                               | 4.18                         | 1.39                             | 5.07                                | 10.06                                  | 13.54                       | 16.7                             |
| S3 / 32                               | 2.72                         | 1.29                             | 4.98                                | 10.17                                  | 13.43                       | 16.36                            |
| S4 / 22                               | 2.45                         | 1.29                             | 4.97                                | 10.2                                   | 13.45                       | 16.13                            |
| All night 225                         | 4.29                         | 1.44                             | 5.06                                | 9.92                                   | 13.49                       | 17.51                            |

## Methodology

Subject of the present study was a healthy male subject aged 31 with body mass index 32 kg/m<sup>2</sup>. The subject was examined by means of conventional PSG including continuous monitoring of EEG (C3A2 derivation) and ECG. Genuine sleep stages were initially detected by means of standard PSG evaluation software (ALICE-4 Respironics) and then reassessed by an expert. The sampling rate of EEG was 100 Hz while that of ECG was 500 Hz.

HRV was assessed from a series of RR-intervals (= time distance between subsequent R-peaks in ECG). The RR-intervals were extracted by a well tested algorithm used for clinical purposes in the Institute of Psychophysiology and Rehabilitation (Palanga, Lithuania) over decades. Subsequently the series of RR-intervals were filtered automatically and reassessed manually by an expert to remove ectopic beats, arrhythmic events, and missing data, because the latter may significantly alter the estimation of the power spectral density  $p_H$  of HRV. Since the established sequence of the RR-intervals represents an irregularly time-sampled signal, the sequence was linearly interpolated with frequency  $F_1=3$  Hz. The value of  $F_1$  was chosen to be higher than the highest instantaneous heart rate and sufficiently high that the Nyquist frequency ( $=F_1/2=1.5$  Hz) of HRV-spectrum is not within the frequency range of interest (i.e., up to 0.5 Hz). The interpolation of the RR-sequence is demonstrated in Fig. 1a.



**Fig. 1.** Calculation of spectrum-weighted mean frequencies  $f_w$ . a) Interpolation of RR\*-sequence with subtracted mean. b) Power spectral density  $p_H$  of HRV with indicated  $f_w$  in different spectral ranges (total spectral range  $f_w^t$ , humoral range  $f_w^h$ , sympathetic range  $f_w^s$ , and parasympathetic range  $f_w^p$ ) during different sleep stages: rapid eye movements (REM) at  $t=100$  min. according to Fig. 2c; sleep stage 3 (S3) at  $t=16$  min., and sleep stage 4 (S4) at  $t=48$  min. The stars to the right visualize the relevant locations in the hypnogram from Fig. 2c. c) The corresponding power spectral densities  $p_E$  of EEG with indicated  $f_w$  (total spectral range  $f_w^t$ , delta range  $f_w^\delta$ , theta range  $f_w^\theta$ , alpha range  $f_w^\alpha$ , SMR range  $f_w^{SMR}$ , and beta range  $f_w^\beta$ )

The values of  $p_H$  were estimated in absolute units ( $\text{ms}^2/\text{Hz}$ ) using intervals of 60 s (180 points) with zero overlap, applying Hamming smoothing and zero padding up to 512 points.

Thus the resulting frequency resolution of  $p_H$  was about 0.006 Hz ( $=F_V/512$ ), i.e., sufficiently fine to estimate  $p_H$  in the lowest humoral band (Table 1). In analogy to  $p_H$ , the power spectral density  $p_E$  of EEG was estimated in absolute units ( $\mu V^2/Hz$ ) using intervals of 10 s (1000 points) with 50 % overlap, applying Hamming smoothing and zero padding up to 2048 points. Here the attained frequency resolution was about 0.05 Hz ( $=100 Hz/2048$ ), i.e., sufficiently fine to estimate  $p_E$  in the lowest delta band (Table 1).

Spectrum-weighted frequencies  $f_W$  were assessed for both HRV and EEC according to:

$$f_W = \int_{f_{\min}}^{f_{\max}} f \cdot dA \bigg/ \int_{f_{\min}}^{f_{\max}} dA = \int_{f_{\min}}^{f_{\max}} f \cdot p \cdot df \bigg/ \int_{f_{\min}}^{f_{\max}} p \cdot df, \quad (1)$$

where  $f$  is the frequency,  $f_{\min}$  and  $f_{\max}$  are the lower and upper bounds of the relevant frequency range, respectively, and  $A$  is the area encompassed by  $p$ , i.e., by  $p_H$  or  $p_E$  (Fig. 1b, c). It can be derived from Eq. 1 that  $f_W$  represents the frequency of the center of  $A$  in the given frequency range  $[f_{\min}, f_{\max}]$ . The values of  $f_W$  were assessed for different frequency ranges, according to Table 1. The chosen ranges are widely accepted for HRV and EEG analysis in the clinical and research fields, and correspond to a particular physiological activity or sleep state [1]. The particular frequency range is given in the superscript of  $f_W$  according to Table 1.

Stationary RR-intervals were visually extracted by an expert before statistical measures of  $f_W$  (means, cross-correlation coefficients) were estimated (Table 1, 2). The resulting lengths of the stationary intervals per sleep stage are given in the first column of Table 1.

## Results

Fig. 1b provides the course of  $p_H$  during three selected sleep stages (REM, S3, and S4). The stage is indicated in the right upper corner of each subfigure. Correspondingly, Fig. 2c illustrates the total sleep profile of the subject with indicated locations of the shown cases in Fig. 1b, c. It can be observed that during the active sleep stage REM the sympathetic activity prevails, whereas during the deepest sleep stage S4 the parasympathetic activity outweighs. The corresponding courses of  $p_E$  during the latter stages are given in Fig. 1c. For instance, it demonstrates that S4 is dominated by delta waves.

The locations of calculated  $f_W$  are indicated by thick vertical lines in each subfigure of Fig. 1b, c. It indicates that  $f_W^t$ , i.e.,  $f_W$  concerning the total spectral range of HRV, strongly increases from REM to S4 by more than 100 % in the depicted case (Fig. 1b). Other changes – some of them being less significant – are summarized in Table 1. It shows absolute mean values of  $f_W$  considering separately particular sleep stages and the whole night. The observations can be given as follows:

- i)  $f_W^t$  showed an increase by more than 70 % from AW (or REM) to S4 (e.g., 0.07 Hz/0.13 Hz for AW/S4),
- ii)  $f_W^h$  concerning the humoral spectral range was nearly constant over all sleep stages ( $=0.03$  Hz),
- iii)  $f_W^s$  concerning the sympathetic spectral range indicated a slight decrease of about 10 % from AW to other sleep stages (e.g., 0.1 Hz/0.09 Hz for AW/S2),
- iv)  $f_W^p$  concerning the parasympathetic spectral range showed a slight increase of about 4 % from AW to deep sleep stages (e.g., 0.19 Hz/0.2 Hz for AW/S4).

Fig. 1c demonstrates that  $f_W^t$ , i.e.,  $f_W$  concerning the total spectral range of EEG, strongly decreases from REM to S4 by more than 70 % in the given case. In parallel, the values  $f_W^b$  seem to decrease by about 15 %. The observations are summarized in Table 1, to give:

- i)  $f_w^t$  showed a decrease by more than 60 % from AW to S4 (e.g., 6.8 Hz/2.4 Hz for AW/S4),
- ii)  $f_w^\delta$  concerning the delta spectral range showed a slight decrease of about 7 % from AW to deep sleep stages with REM showing the highest values (e.g., 1.6 Hz/1.3 Hz for REM/S4),
- iii)  $f_w^\theta$  concerning the theta spectral range showed no significant changes over all sleep stages (=5 Hz),
- iv)  $f_w^\alpha$  concerning the alpha spectral range showed a slight decrease of about 6 % from AW to REM with other sleep stages S1-S4 showing no decrease in comparison with AW (e.g., 10.1 Hz/9.5 Hz for AW/REM),
- v)  $f_w^{SMR}$  concerning the SMR spectral range showed no significant changes over all sleep stages (=13.5 Hz), and
- vi)  $f_w^\beta$  showed a decrease by about 20 % from AW (or REM) to S4 (e.g., 20.4 Hz/16.1 Hz for AW/S4).

Fig. 2a, b presents the time courses of a few selected  $f_w$  from HRV and EEG while the corresponding sleep staging (= hypnogram) is given in Fig. 2c. It is interesting to observe that  $f_w^t$  indicates an inverse behaviour to the hypnogram, deep sleep stages corresponding to increased values of  $f_w^t$  and reduced values to shallow (or active) sleep stages. This observation is in good agreement with the aforementioned data in Table 1. In analogy, the course of  $f_w^\alpha$  is also inversely related to the hypnogram while that of  $f_w^\delta$  and  $f_w^t$  show slight similarities with the hypnogram.

The resulting cross-correlation coefficients between  $f_w$  from HRV and that from EEG are given in Table 2. Here the total night as well as AW and S4 stages are considered. The white background of the cells indicates statistically significant correlations, the significance level being given below the table. The following observations can be made:

- i) Stage AW demonstrated a strong negative correlation between  $f_w^h$  and  $f_w^\alpha$ , i.e., increases of  $f_w^h$  were interrelated with decreases of  $f_w^\alpha$  and vice versa. In addition, a negative correlation is obvious between  $f_w^t$  and  $f_w^p$ .
- ii) Stage S4 showed a strong negative correlation between  $f_w^t$  and, on the other hand,  $f_w^t$  and  $f_w^\delta$ .
- iii) The total night record revealed a negative correlation between  $f_w^t$  and, on the other hand,  $f_w^t$  and  $f_w^\beta$ , which was already indicated in Fig. 2a, b. A weak positive correlation was given between  $f_w^t$  and  $f_w^\alpha$ .

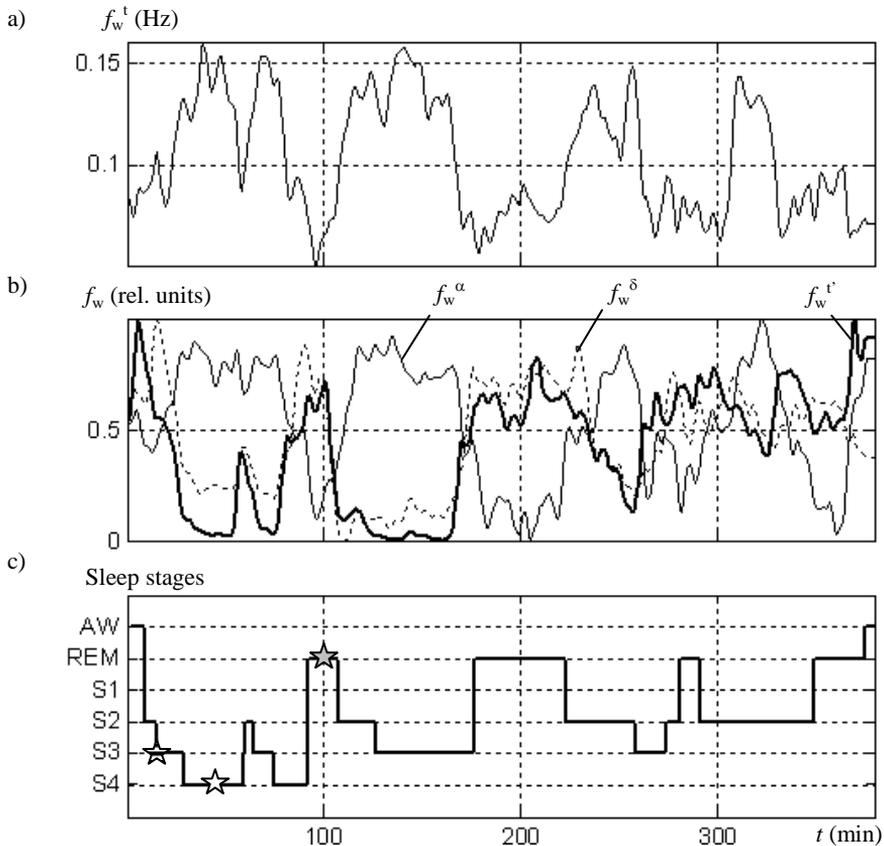
**Table 2.** Cross-correlation coefficients of weighted mean frequencies  $f_w$  from HRV and EEG for awake (AW), deep sleep stage 4 (S4), and all night (AN) concerning different spectral ranges.

| Spectral ranges for EEG | Spectral ranges for HRV |       |       |                     |       |       |                         |       |       |                             |       |       |
|-------------------------|-------------------------|-------|-------|---------------------|-------|-------|-------------------------|-------|-------|-----------------------------|-------|-------|
|                         | Total ( $f_w^t$ )       |       |       | Humoral ( $f_w^h$ ) |       |       | Sympathetic ( $f_w^s$ ) |       |       | Parasympathetic ( $f_w^p$ ) |       |       |
|                         | AW*                     | S4*   | AN**  | AW*                 | S4*   | AN**  | AW*                     | S4*   | AN**  | AW*                         | S4*   | AN**  |
| Total ( $f_w^t$ )       | 0.25                    | -0.72 | -0.61 | -0.48               | 0.05  | -0.07 | 0.61                    | -0.23 | 0.03  | -0.76                       | 0.08  | 0.09  |
| Delta ( $f_w^\delta$ )  | 0.19                    | -0.72 | -0.49 | 0.06                | 0.12  | -0.08 | 0.46                    | -0.32 | -0.05 | -0.45                       | 0.07  | 0.07  |
| Theta ( $f_w^\theta$ )  | 0.15                    | -0.08 | -0.11 | -0.37               | -0.30 | -0.02 | 0.35                    | -0.01 | 0.12  | -0.19                       | 0.10  | -0.01 |
| Alpha ( $f_w^\alpha$ )  | -0.19                   | 0.35  | 0.54  | -0.72               | -0.21 | 0.17  | 0.08                    | 0.14  | 0.07  | -0.30                       | -0.10 | -0.37 |
| SMR ( $f_w^{SMR}$ )     | -0.38                   | -0.15 | -0.23 | -0.50               | 0.11  | -0.06 | 0.22                    | 0.07  | 0.00  | 0.14                        | 0.29  | 0.00  |
| Beta ( $f_w^\beta$ )    | 0.15                    | -0.10 | -0.58 | 0.06                | 0.03  | -0.17 | 0.28                    | -0.10 | 0.04  | -0.09                       | 0.36  | 0.29  |

\* grey background indicates that hypothesis of no correlation accepted with > 95 %.

\*\* grey background indicates that hypothesis of no correlation accepted with > 99 %.

For the sake of completeness, it should be mentioned that the stage S3 indicated correlations which are very similar to that from stage S4. This may be due to the fact that both stages represent deep sleep stages. The stage S2 revealed only very weak correlation coefficients (though significant), their absolute value not exceeding 0.5. The significant coefficients from the stage REM were even lower. The stage S1 showed no stationary RR-intervals (Table 1), thus no correlations were calculated here.



**Fig. 2.** Courses of spectrum-weighted mean frequencies  $f_w$  over the night. a)  $f_w^t$  of HRV concerning total spectral range. b)  $f_w$  of EEG concerning total spectral range  $f_w^t$ , delta range  $f_w^\delta$ , and alpha range  $f_w^\alpha$ . c) The corresponding hypnogram showing sleep stages over night (AW awake, REM rapid eye movements, S1-S4 sleep stages from drowsy to deep sleep). The stars denote time instants related to the data depicted in Fig. 1b, c

## Discussion

The present case study investigates the relation of the spectrum-weighted frequencies  $f_w$  of HRV and EEG for different widely-established spectral ranges and for different sleep stages. It demonstrates numerous interrelations, the strongest inverse relation being given between  $f_w$  of the total spectral range of HRV and that of EEG. Interestingly, the latter  $f_w$  are even

approximately related to the sleep profile of the study subject, i.e., they have a predictive value in identifying shallow sleep versus deep sleep.

Selected spectral ranges revealed lower correlations, which may be due to the strict (or narrow) band limits while calculating  $f_w$  in the light of non-zero values of the power spectral density  $p$  at band limits. For instance, an implication of such restriction can be observed in Fig. 1b, where maxima of  $p$  are not exactly matched by calculated  $f_w$ . Furthermore, an obvious restriction of the given study is that only data from a single subject was used. The statistical relevance of  $f_w$ , e.g., their predictive value of sleep architecture, should be verified in future using extensive data bases.

However, the present case study has demonstrated a relationship between HRV and EEG in different sleep stages suggesting a close dependence of autonomic cardiovascular control on central nervous system. The methodology of the spectrum-weighted frequencies may even help assess the quality of sleep, e.g., fraction of deep sleep stages. The sleep-related relation of HRV-measures and EEG-measures emphasizes the importance and usability of the HRV-analysis in sleep studies, since EEG is considered as a standard for sleep staging. In praxis, it may be very attractive to roughly assess the sleep architecture in a very simple and comfortable way, e.g., by using only a single ECG-signal, which is relevant for many medical areas.

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