

# Detrended Fluctuation Analysis and Spectral Analysis of Heart Rate Variability for Sleep Stage and Sleep Apnea Identification

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## Abstract

*In a systematic study we compared the performance of spectral analysis and detrended fluctuation analysis (DFA) to discriminate sleep stages and sleep apnea.*

*We investigated 14 healthy subjects, 33 patients with moderate, and 31 patients with severe sleep apnea with polysomnography.*

*Discriminance analysis was used on a person and sleep stage basis to determine the best method for the separation of sleep stages and sleep apnea severity. Using spectral parameters 69.7% of the apnea severity assignments and 54.6% of the sleep stage assignments were correct, while using scaling analysis these numbers increased to 74.4% and 85.0%, respectively. Changes in heart rate variability are better quantified by scaling analysis than by spectral analysis.*

## 1. Introduction

Sleep as the absence of wakefulness and the missing ability to react on external stimuli is regarded as a unbiased test situation for the autonomic nervous system [1]. Sleep is not just a constant state controlled by metabolic needs for the body being at rest. Instead sleep consists of different well defined sleep stages which follow a well structured temporal order in normal restorative sleep. Heart rate and heart rate variability vary with the sleep stages, and their normal variability is affected in sleep disorders. It has been shown that autonomic activity changes from waking to sleep. Big differences were found between non-REM and REM sleep [2]. Sympathetic tone drops progressively from wakefulness over sleep stage 1 to 4. In contrast REM sleep was characterized by increased sympathetic tone [3]. Parasympathetic tone increases from wakefulness to non-REM sleep. Periods of wakefulness during sleep were found to have an intermediate position between non-REM and REM sleep [4].

Sleep apnea affects heart rate variability during sleep described as cyclical variation of heart rate [5]. The recording of cyclical variation of heart rate together with snoring has been used in order to detect obstructive sleep apnea with ambulatory recording devices [6]. It can be

assumed that the cyclical variation of heart rate can be detected by spectral analysis if the appropriate frequency range is investigated. The pattern of bradycardia and tachycardia during apnea has been attributed to an effective parasympathetic control of heart rate during sleep [7] interrupted by sympathetic activation accompanying the intermittent apnea-terminating arousals.

Spectral analysis of heart rate variability is well established and provides a quantitative evaluation of sympathetic and parasympathetic activation of the heartbeat [8]. Three major oscillatory components were identified. The physiological interpretation of the very-low-frequency (VLF) component ( $< 0.04$  Hz) is still discussed, the low-frequency (LF) component (0.04 – 0.15 Hz) reflects baroreflex sympathetic control of blood pressure, and the high-frequency (HF) component (0.15 – 0.4 Hz) reflects respiratory rhythm and is believed to be related to parasympathetic control of heart rate [9].

Detrended fluctuation analysis (DFA) method has become a widely-used technique for the detection of long-range correlations in noisy, non-stationary time series. In the DFA method, long-range correlations between interbeat intervals separated by several beats are detected by investigating the scaling behavior of the heartbeat fluctuations on different time scales disregarding trends and non-stationarities in the data [10].

This study was performed on existing sleep recordings to compare spectral analysis of heart rate and DFA in their ability to distinguish sleep stages in normal and sleep apnea subjects. We also wanted to see whether sleep apnea severity can be distinguished using parameters derived from spectral analysis and DFA and which one performs better.

## 2. Methods

Sixty-four patients with symptoms of excessive daytime sleepiness and arterial hypertension were recruited. Patients had to be free of any cardiovascular medication. Patients with apparent cardiac arrhythmias were excluded. 33 patients with mild to moderate obstructive sleep apnea with an apnea-hypopnea index AHI  $< 40$  events/hour and 31 patients with severe sleep apnea AHI  $> 40$  events/hour were selected for this study.

Table 1. Results of sleep stage scoring and evaluation of breathing are given for healthy persons and the two sleep apnea groups. Body mass index (BMI), apnea-hypopnea index (AHI) and total sleep time (TST) are listed.

	healthy	moderate sleep apnea	severe sleep apnea
subjects (n)	14	33	31
age (years)	33.0 ± 6.4	47.9 ± 9.1	50.0 ± 8.0
BMI (kg/m <sup>2</sup> )	21.7 ± 2.4	28.4 ± 4.2	33.7 ± 6.7
AHI (n/h)	0.6 ± 1.4	19.0 ± 8.0	65.1 ± 18.4
TST (min)	393 ± 37	361 ± 42	358 ± 49
wake (min)	64 ± 27	98 ± 45	103 ± 45
light sleep (min)	248 ± 39	235 ± 41	281 ± 40
deep sleep (min)	58 ± 19	50 ± 28	11 ± 16
REM sleep (min)	87 ± 23	75 ± 27	66 ± 21

In order to compare our results with normal subjects 14 healthy persons participated in the study. These normal controls had no symptoms of sleepiness and no sleep apnea.

All subjects underwent two subsequent nights of polysomnography with EEG, EOG, EMG, recording of oro-nasal airflow, respiratory movements, snoring, oxygen saturation, and ECG as required for sleep studies [11]. Sleep was evaluated according to Rechtschaffen and Kales. For subsequent analysis some sleep stages were grouped together. We distinguished 'light sleep' (stage 1 and 2), 'deep sleep' (stage 3 and 4), 'REM sleep', and 'wakefulness'.

Together with the other signals ECG lead II had been digitized at 100 Hz for patients and 200 Hz for normal subjects. The interbeat intervals were derived from the ECG as RR intervals using an R-wave detector. The time series were obtained for the entire duration of the sleep recording. All annotated periods of wakefulness, light sleep, deep sleep and REM sleep were analyzed separately.

Based on discussions with our cardiologist on arrhythmia related artifacts in interbeat time series we chose the following practical criteria for automatic preprocessing: sleep recordings from our patients were excluded from our retrospective analysis, if more than one percent of the interbeat intervals failed to meet the following criteria:  $0.33 \text{ s} < \text{interbeat interval} < 1.5 \text{ s}$  and  $0.66 \text{ s}$  maximum difference from the previous interbeat interval. All recording epochs, where one sleep stage persisted shorter than 3 minutes or had more than one percent of RR intervals violating the criteria were excluded. In addition, the violating intervals in accepted epochs were also excluded, concatenating the remaining parts of the series.

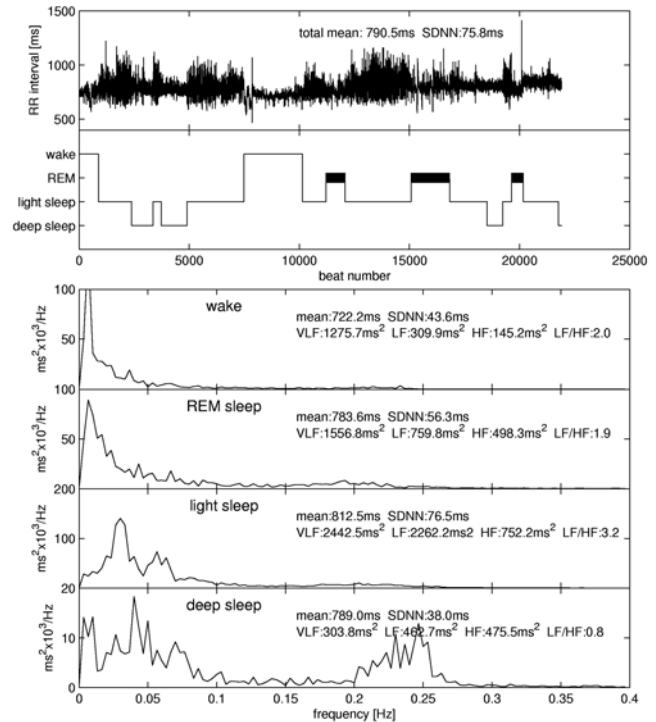


Fig. 1. The calculation of the spectral parameters using FFT in 5 minute segments was performed separately for the sleep stages. The summed spectra for each sleep stage were plotted and used to calculate the spectral bands. The figure depicts the heart rate and the sleep stage records as well as the power spectra for light sleep, deep sleep, REM sleep, and wake for a patient with moderate sleep apnea. For the spectra the y-axis for light sleep has a different scale in order to show the pronounced VLF peak being characteristic for sleep apnea during light sleep.

In order to investigate 'clean' sleep stage effects on heart rate variability without sleep stage transition effects and non-stationarities associated with them we removed the initial and the final 45 seconds of each sleep stage period. Time domain and frequency domain measures were calculated according to standard definitions [9]. Mean RR intervals and the standard deviation of all RR intervals (SDNN) were calculated in the time domain.

For the calculation of the power spectra, the RR interval time series was resampled at 3.41 Hz using linear interpolation. Consecutive segments of 5 minutes (1024 points) inside each sleep stage were analyzed by spectral analysis (FFT) separately. We calculated total power, VLF ( $\leq 0.04 \text{ Hz}$ ), LF (0.04 – 0.15 Hz), HF (0.15 – 0.4 Hz) and the ratio LF/HF for the individual sleep stages separately.

The detrended fluctuation analysis is calculated as the average over all segments and takes the square root to obtain the fluctuation function  $F(t)$ :

$$F(t) \equiv \left[ \frac{1}{2N_t} \sum_{v=1}^{2N_t} F_t^2(v) \right]^{1/2}.$$

It is apparent that  $F(t)$  will increase with increasing  $t$ , since the deviations from the fits will become larger for larger segments. If the data are long-range power-law correlated,  $F(t)$  increases, for large values of  $t$ , as a power-law,

$$F(t) \sim t^\alpha.$$

When the fluctuation function  $F(t)$  is plotted as a function of  $t$  on double logarithmic scales, the fluctuation scaling exponent  $\alpha$  can be determined by a linear fit. For uncorrelated data, the scaling exponent is  $\alpha = 0.5$ . For short-range correlated data  $\alpha$  is larger than 0.5 on small scales  $t$ , but a crossover to  $\alpha = 0.5$  is observed on large scales  $t$ . Power-law behavior with  $\alpha > 0.5$  on large scales  $t$  indicates long-range correlations in the data.

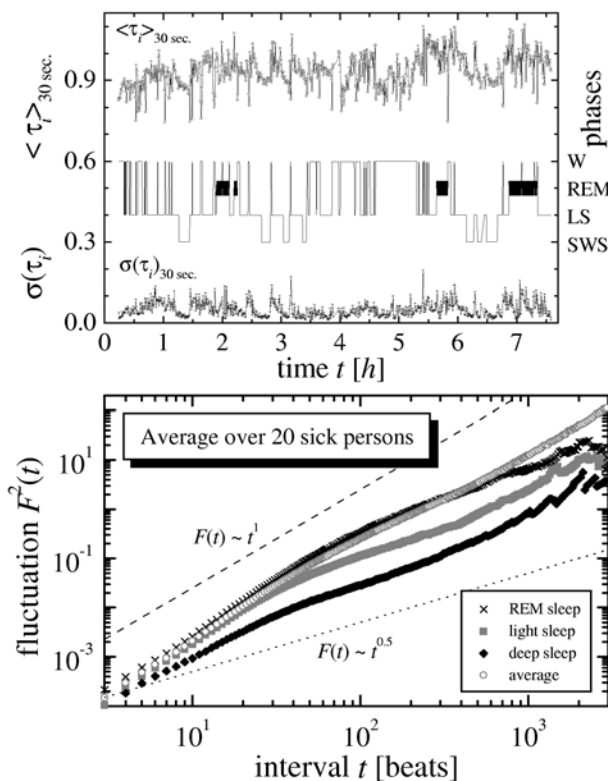


Fig 2. The top part illustrates the disturbed heart rate together with the sleep stages of a patient with sleep apnea. The lower part depicts the DFA in double-logarithmic plot as a mean value for 20 subjects with sleep apnea. The different slopes for the sleep stages can be observed.

Differences between sleep stages with the classes 'light sleep', 'deep sleep', 'REM sleep', 'wake' and differences in

sleep apnea severity with the classes 'normal', 'mild to moderate, AHI < 40', 'severe, AHI > 40 events/hour', were tested for two sets of dependent variables. The dependent variables were mean RR intervals, SDNN, VLF, LF, HF, and LF/HF in the first set and mean RR intervals, SDNN,  $\alpha_1$ ,  $\alpha_2$  calculated with DFA2 in the second set. A multiple analysis of variance (MANOVA) was applied for both sets. In order to check the differences between the individual groups Bonferroni tests were applied afterwards for both sets. Statistical significance was stated for  $p < 0.05$ . The statistical test was performed by SPSS version 10 (SPSS Inc, Chicago IL, USA).

In order to compare the set of parameters derived by spectral analysis with the set of parameters given by DFA to determine their ability to discriminate between sleep stages and between differences in severity of sleep apnea we choose discriminant analysis. As parameters derived by DFA we choose  $\alpha_1$  and  $\alpha_2$  calculated with DFA2 as used in the MANOVA. From the spectral analysis we choose the variables VLF, LF, HF, and LF/HF as used in the MANOVA. The target variables for sleep were 'light sleep', 'deep sleep', 'REM sleep', and 'wake' derived for each subject and for apnea were 'normal', AHI < 40, and AHI > 40 events/hour. The model derived by discriminant analysis creates hyperplanes in the hyperspace. The hyperplanes for the independent variables were applied to predict the correct assignment of each single subject into the corresponding class of sleep and apnea – corresponding to the segment in the hyperspace. The numbers of correct assignments were calculated in percent.

### 3. Results

By applying discriminant analysis which separates the hyperspace created by the dependent parameters with hyperplanes we could prove that separation of sleep stages was performed best using  $\alpha_1$  and  $\alpha_2$  derived by DFA. 78.4% of sleep assignments were correct. If mean RR intervals and SDNN were added, the correct assignments increased to 85.0%. The assignments of sleep stages based on spectral analysis parameters resulted in 51.4%. If mean RR interval and SDNN were added 54.6% of correct assignments were reached for sleep stages.

Separation of apnea severity based on spectral parameters performed better than based on DFA parameters. 63.6% of apnea severity assignments were correct. If mean RR intervals and SDNN were added to the discriminant analysis model, the correct assignments increased to 69.7%. The assignments of apnea severity based on DFA parameters resulted in 60.1%. If mean RR interval and SDNN were added 74.4% of assignments were correct. This was slightly better than the spectral parameter set together with time domain parameters.

If both classes were separated at the same time, and the corresponding discriminant model was applied, DFA analysis was better with 54.9% of correct assignments compared to spectral parameters with 36.3% correct assignments. In both cases, mean RR intervals and SDNN were included in the model.

As a last test, all variables, derived by DFA, the spectral parameters, mean RR intervals, and SDNN were taken together. Then we achieved 84.1% correct assignments for sleep, 72.9% for apnea and 56.1% for separating both classes at the same time.

#### 4. Discussion

This is the first study which systematically compared the method of spectral analysis of heart rate variability and DFA in a group with a defined disorder of high interest. We used both methods to compare the ability to discriminate sleep stages and sleep apnea severity. The separation of sleep stages was performed best using the two parameters derived by DFA together with time domain measures. The separation of apnea severity was also better using the parameters derived by DFA taken together with time domain measures. If only spectral parameters were compared to DFA parameters, they were better in the case of apnea severity. The results indicate that DFA derived parameters reflect heart rate regulation properties which complement time domain measures and their combination performs better than spectral measures when we want to distinguish sleep stage and apnea severity.

A limitation of our study is, that the age and body mass index of our healthy control subjects (employees of the hospital) is considerably lower than age and body mass index of our patients. Both factors play a role in heart rate regulation. Our patients had no other cardiac or pulmonary disorder beside sleep apnea. These other disorders were excluded prior to the study. The patients with sleep apnea had an elevated office blood pressure at the time of being recruited for this study.

Age and body mass index are very typical for sleep apnea patients. As the influence of age and body mass index on our results cannot be completely excluded this presents a limitation of our study. This specific limitation is a very common limitation to most studies on sleep disordered breathing.

Our results do indicate that it might be possible to improve heart rate analysis in such a way that it is possible to recognize the severity of sleep apnea in rough classes as had been used here and sleep stages in a general way which distinguishes wake, light sleep, deep sleep and REM sleep. In order to prove these hypotheses prospective studies with implementations of the discriminance functions must be performed on subjects with sleep disordered breathing as well as in subjects which suffer from other disorders affecting the autonomic system.

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