Circadian Behavior of Cardiovascular Variability

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Abstract—**The autonomous nervous system is modulated by the sleep-wake cycle and the circadian system at the same time. In order to investigate the separate circadian influence on noninvasive parameters of the cardiovascular variability which could reflect the state of the autonomic tone, we applied a 40-hours constant routine protocol on twelve healthy young volunteers. During that period continuous multi-channel recordings of EKG, EEG, EOG, EMG and respiration were performed. Out of the EKG, sampled with 512 Hz, time domain as well as frequency domain heart rate variability parameters were calculated time-variant in 15-min bins. Descriptive analysis of results revealed a clear circadian modulation of the parameters of the cardiovascular variability. Additionally effects induced by the experimental setting were observed. The findings could make contribution in the design of a noninvasive autonomic state index measure which could be used in patients as well as for daily work life conditions.**

Keywords— **Cardiovascular Variability, Heart Rate Variability, Autonomous Nervous System, Circadian System, Sleep**

I. Introduction

The autonomous nervous system is connected with sleep-wake regulating structures and at the same time modulated by circadian factors [1-2]. It is also known, that different medical conditions, exercise and environmental factors lead to an elevated activity of the autonomous nervous system.

In recent years, a number of measures of cardiovascular variability (CVV) were explored who are able to reflect the state of the cardiac autonomic tone [3]. Especially parameters of heart rate variability (HRV) have become one of the most prominent noninvasive markers of CVV. In this context several linear and non-linear analysis approaches are available in the time as well as in the frequency domain.

In order to investigate the independent influence of the internal circadian clock on the CVV without influences of any kind of disease or stages of sleep we applied continuous analysis of HRV out of multi-channel bio-signal recordings under 40 hours of constant routine conditions in healthy volunteers.

II. Methods

Twelve healthy young male students (mean age 24.9±3.2 years) were recruited to participate in a constant routine (CR) protocol in a sleep lab. The CR conditions for the volunteers included to stay awake for 40-hours and at the same time to be excluded from all external clocks, to have regular food intake, to be under constant dim light, to lie in a supine position, as well as to perform certain tests for performance, alertness, language processing, and others repetitively. Body temperature as well as saliva melatonin concentration was measured as reference circadian markers. In order to guarantee similar CR startup conditions all volunteers slept one night in the sleep lab prior to the CR. The CR started for all volunteers at 08.00 hours in the morning.

During the whole CR continuous polysomnographic recordings were performed with an *Embla N7000 recorder* (Embla systems, Broomfield, CO, USA) including EKG, respiration, EEG, EMG, and EOG measurements. EKG (lead II) was sampled with 512 Hz and offline filtered using a Butterworth bandpass (0.3-70 Hz). Beat-to-beat time series of RR intervals were determined using R-peak-detection algorithm. A semi-automatical algorithm for detection and elimination of artifacts (noise, body movements, extrasystolic beats) was applied. Calculation of time-variant HRV indices was performed for subsequent 15minute bins.

In the time domain, the mean heart rate (HR), the Standard Deviation of Successive Differences (SDNN), and the Root Mean Square of Successive Differences (RMSSD) were calculated. Based on a 12 pole AR spectrum in the frequency domain the Very Low Frequency (VLF), the Low Frequency (LF), the High Frequency (HF), and the Total Power (TP) spectral bands were calculated. All data preprocessing and analysis was done according to the Task Force on HRV standards [4] using the software *Somnologica Science 3.3.1* (Embla systems, Broomfield, CO, USA).

O. Dössel and W.C. Schlegel (Eds.): WC 2009, IFMBE Proceedings 25/VII, pp. 516–518, 2009.
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III. Results

Out of the 12 volunteers who were included in the CR 11 of them completed the whole 40 hours CR protocol. The EKG recordings of the 11 remaining data sets (approximately 144.000 beats per subject) were analyzed. Descriptive data analysis was applied to the time-variant HRV indices. Results of group mean±SD values together with body temperature and melatonin concentration curves were plotted with respect to the start of the CR.

For the HR as well as for the HRV parameters in the time domain and also in the frequency domain time of day fluctuations were observed.

Individual analysis revealed that circadian patterns were present in 82% of the analyzed volunteers. Parameters showed a vice versa behavior with respect to temperature with a nadir approximately at 20.00 hours and a peak at 04.00 hours the next day (Fig. 1 and 2).

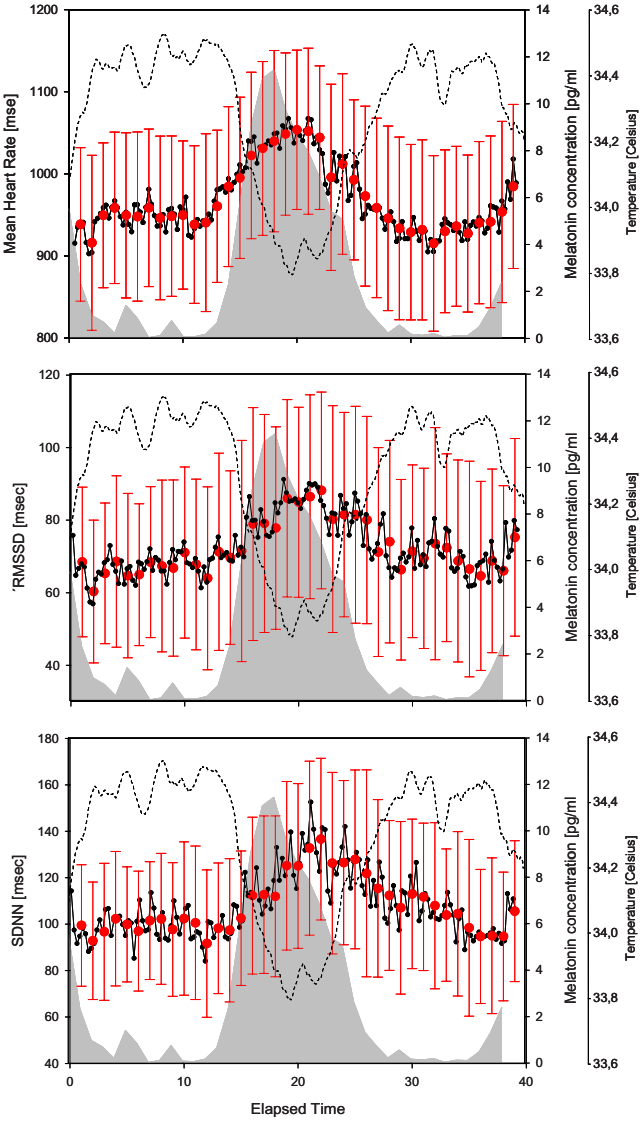

Fig. 1 Mean±SD time domain HRV parameters for the 40-hour constant routine (CR) period with respect to body temperature (dotted line) and melatonin concentration levels (filled area)

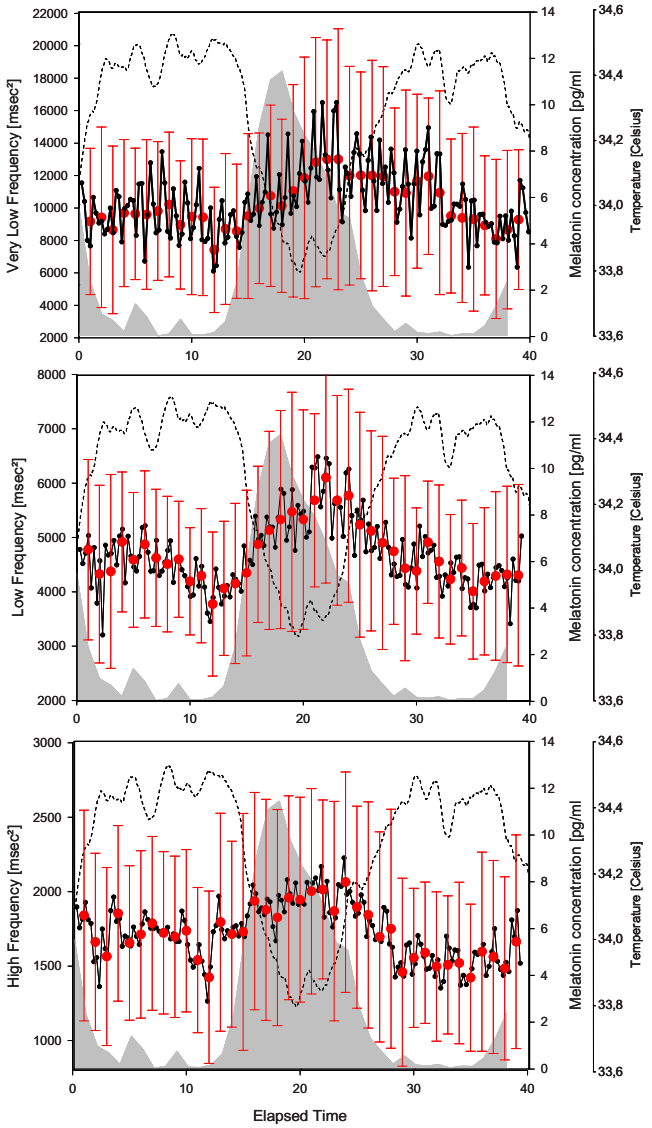

Fig. 2 Mean±SD frequency domain HRV parameters for the 40-hour constant routine (CR) period with respect to body temperature (dotted line) and melatonin concentration levels (filled area)

For the HR we found a minimum in the late afternoon with an increase of approximately 115 msec at about 04.00 hours the next day. For SDNN – a parameter of the global variability – also a maximum in the early morning hours was found (Fig.1).

For the parameters out of the spectral analysis we found for the LF as well as HF components a maximum in the morning hours of the 2nd day between 03.00 hours and 05.00 hours with remaining higher levels at the subsequent daytime hours. A modulation of parameters –especially for the VLF component - with duration of approximately 1 hour was observed. This parameter variation was induced by the experimental setting since most additional tests (for vigilance, alertness, etc.) were repeated every hour (Fig.2).

IV. Discussion

The analysis of parameters of CVV under CR conditions allows insights into the regulation of the autonomous nervous system. The observed circadian modulation of the time domain as well as the frequency domain HRV parameters indicates a sleep-wake state independent behavior of the autonomic tone and the results are in the same direction with findings of others [5]. A remaining question is the influence of the degree of sleepiness as well as alertness and vigilance on those parameters. The remaining higher levels of the LF and HF components observed at the 2nd day of the CR together with expected diminished alertness and vigilance values supports the assumption of such an additional effect on the CVV.

In summary, the results of this CR study could contribute for a design of an autonomic state index measurement concept which could be used in the clinical setting as well as for daily work life studies like shift work conditions.

Acknowledgment

A financial support for this study was provided by the Gottlieb-Daimler-and-Karl-Benz Foundation, Ladenburg, Germany.

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