

Temporal relationship between dynamic heart rate variability and electroencephalographic activity during sleep in man

H. Otzenberger*, C. Simon, C. Gronfier, G. Brandenberger

UPRES 12, Faculté de Médecine, 67085 Strasbourg cedex, France

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Abstract

In previous sleep studies, it has been demonstrated that Poincaré plots of RR intervals, which provide a beat to beat dynamic measure of heart rate variability, have distinctive and characteristic patterns according to sleep stages. This study was designed to evaluate the temporal relationship between heart rate variability and sleep electroencephalographic activity (EEG) by using the Pearson's interbeat autocorrelation coefficients of RR intervals derived from the Poincaré plots. The coefficients were calculated in 12 subjects over each minute and were related to the profiles of EEG mean frequency (0.5–35 Hz) computed using a Fast Fourier Transformation algorithm. Overnight profiles of interbeat autocorrelation coefficients and of EEG mean frequency were found to be related with highly significant cross-correlation coefficients ranging between 0.216 and 0.638 ($P < 0.001$). The variations in heart rate variability preceded changes in brain activity by 1–2 min. These results demonstrate that beat to beat heart rate variability and EEG activity are closely linked during sleep in normal man. © 1997 Elsevier Science Ireland Ltd.

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Numerous studies have documented the variation of heart rate during sleep. An overnight declining trend has been reported with superimposed increases during rapid eye movement (REM) sleep as compared to subsequent non-(N)REM sleep [5,14]. The Poincaré plot method is a non-linear procedure which allows a beat to beat measure of heart rate variability [7]. This procedure based on a scatterplot of current RR interval against the previous RR interval gives information on instantaneous heart rate variability in a compact visual format which can be readily interpreted in a qualitative manner. This procedure has been used to identify abnormalities of cardiac dynamic rhythms in numerous pathological conditions including sudden infant death syndrome and heart failure [13,15,19]. In previous sleep studies, it has been demonstrated in man [9,17,18,20] as well as in animals [11] that the cardiac Poincaré plots, based on 5–20 min sleep recording, have distinctive and characteristic

patterns according to sleep stages with REM sleep characterised by more regulated interbeat variability despite higher overall variations as compared to NREM sleep. All these previous studies were performed using the traditional classification of sleep stages based on visual pattern recognition [12]. Spectral analysis of the sleep electroencephalogram (EEG) by means of Fast Fourier Transformation (FFT) is a more useful tool which allows a quantitative analysis of the sleep EEG and a more precise description of the sleep processes to be obtained [1].

The aim of the present study was to evaluate the temporal relationship between the overnight profiles in EEG activity and in heart rate variability, as evaluated by interbeat autocorrelation coefficient (rRR) derived from the Poincaré plots. The interbeat autocorrelation coefficients were calculated over each minute during the sleep period and their overnight profiles were established for the first time as an index of dynamic heart rate variability. Their successive values were plotted with regard to variations of EEG mean frequency, reflecting variations in sleep depth, so that the synchrony between brain activity and heart rate variability could be accurately estimated.

* Corresponding author. Laboratoire de Physiologie et de Psychologie Environnementales (CNRS), 21 rue Becquerel, 67087 Strasbourg Cedex, France. Tel.: +33 3 88106757; fax: 33 3 88106245; e-mail: helene.otzenberger@c-strasbourg.fr

Twelve healthy male subjects between 21 and 28 years of age volunteered for the study. They participated in the study after medical examination and screening tests. All had regular sleep-wake habits and none was taking any medication. Informed written consent was obtained from all of them and the experiment was approved by the local Ethics Committee. The experiments were carried out in a sound proof air-conditioned sleep room. After a habituation night in the laboratory, each subject underwent an experimental night during which sleep and cardiac recordings were carried out. Lights were switched off at 2300 h and the subjects were awakened at 0700 h. Electrodes were attached 2 h before the beginning of the recordings. All EEG signals were high-pass filtered at 0.3 Hz (6 db/oct) and low-pass filtered at 35 Hz (6 db/oct). Sleep stages were scored visually from the polygraphic recordings according to Rechtschaffen and Kales criteria [12]. An all-night spectral analysis was performed by converting the EEG signal (derivations C3-A2 or C4-A1) from analog to digital with a sampling frequency of 128 Hz. Subsequently, spectra were computed for all consecutive 2-s periods using a FFT algorithm [6]. In order to yield 1 min power density values, the median was calculated for each 30 consecutive 2-s periods. The EEG spectral parameter considered was the mean frequency of the global EEG band (0.5–35 Hz). Heart rate was measured by the electrocardiogram signal fed into a generator which produces a pulse at the rising phase of each R wave. The trigger event times, to an accuracy of ± 1 ms, were recorded and the RR intervals were calculated on a computer equipped with a data acquisition control board including a timer. Computers and polygraphs were synchronized. Each RR interval was plotted against the previous RR interval to produce a cardiac Poincaré plot (RR_{n+1} versus RR_n) for each minute. The interbeat autocorrelation coefficient of RR intervals (rRR) (i.e. Pearson's correlation coefficient between the RR_n and RR_{n+1}) was calculated over each minute, using the entire unfiltered data.

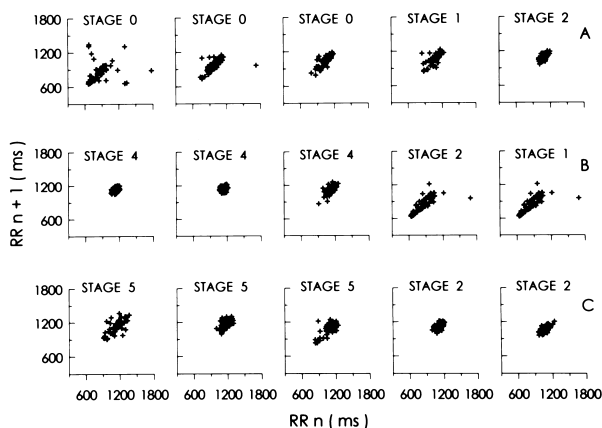


Fig. 1. Examples of successive minute Poincaré plot patterns in one subject during a transition from waking (stage 0) to sleep stage 2 (A); during a transition from stage 4 to stage 1 (B); during a transition from REM sleep (stage 5) to stage 2 (C).

The temporal relationship between rRR and EEG mean frequency was quantified during the sleep periods using cross-correlation analysis. Cross-correlation coefficients and their levels of significance between rRR and EEG mean frequency were computed on row data for lags (-10) to (+10), each lag corresponding to 1-min interval (Box Jenkins Time Series Analysis, BMDP Statistical Software).

Fig. 1 illustrates successive minute Poincaré plots for one subject during sleep onset (Fig. 1A), during a transition from stage 4 to stage 1 (Fig. 1B) and during a transition from REM sleep (stage 5) to stage 2 (Fig. 1C). Each sleep stage presented a characteristic and distinctive pattern of Poincaré plots. During waking periods (stage 0), the scatter of points was spread in the bottom of the left corner, due to short RR intervals (Fig. 1A); the overall shape of point dispersion was long and relatively thin along the diagonal line. During sleep onset (Fig. 1A) the points progressively clustered together and moved off further from the origin reflecting longer RR intervals. Stage 4 was characterized by smaller and rounder clusters of points, reflecting the decrease of overall variation (Fig. 1B). The transition from stage 4 to stage 1 was characterized by a progressive dispersion of the points along the diagonal line. During REM sleep (stage 5), Poincaré plots were spread along the diagonal line with a high overall length, but with a localization far from the origin, because of higher values of RR intervals (Fig. 1C). Again, the transition towards sleep stage 2 was characterized by a progressive clustering of the points.

Fig. 2 illustrates the overnight profiles of rRR and of mean RR intervals calculated over each minute, together with the sleep stage pattern in one representative subject. It shows the cyclic changes in rRR with low levels during NREM sleep and high levels during REM sleep and waking periods. rRR calculated for each minute in the 12 subjects were significantly lower during NREM sleep than during REM sleep (0.37 ± 0.03 versus 0.57 ± 0.04 ; $P < 0.001$). In contrast, RR intervals did not show any systematic variation according to NREM-REM sleep cycles.

Fig. 3 shows two examples of individual rRR profiles with regard to the profiles of EEG mean frequency (0.5–35 Hz). The data were transformed into Z-scores to illustrate the relative variations of the two chronological series. rRR and EEG mean frequency paralleled each other. Cross-correlation analysis between nocturnal profiles of rRR and of EEG mean frequency revealed that both variables were positively correlated in all subjects ($P < 0.001$). The cross-correlation coefficients are given in Table 1. The highest coefficients were found to be significant for lags lying between (-2) and (-1) which indicated that variations in rRR preceded changes in EEG mean frequency by 1–2 min. In contrast, cross-correlation analysis between RR intervals and EEG mean frequency revealed no systematic association between both variables.

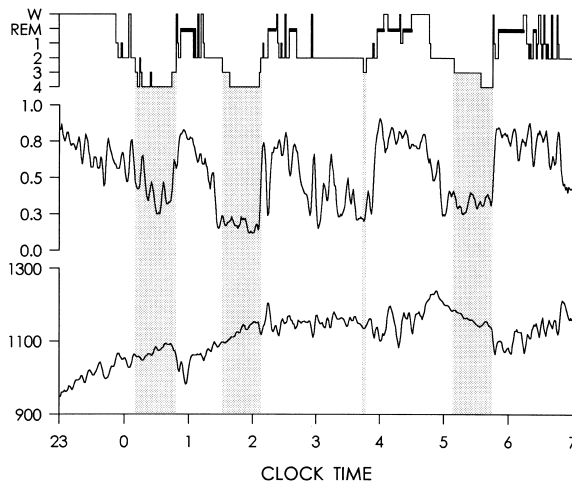


Fig. 2. Profiles of minute interbeat autocorrelation coefficient (rRR) and of RR interval together with sleep stage pattern in one subject. Slow wave sleep (stage 3 and 4) lies in shaded areas. rRR and RR curves were smoothed using the moving average method over a five-point span.

This study demonstrates that minute Poincaré plot of RR intervals, simple to construct, is a useful tool to assess the changes in dynamic heart rate variability that occur during sleep in man. The graphs provide pictures of beat to beat interval behaviour that reveal distinctive patterns for each of the sleep–wake states. The interbeat autocorrelation coefficient of RR intervals (rRR) calculated over each minute gives a new cardiac measure that was used to evaluate the temporal relationship between heart rate variability and variations of EEG activity during sleep. The results show that the overnight profiles of rRR were highly correlated with variations in EEG mean frequency, the heart rate changes preceding the changes of the EEG signals. Increased rRR

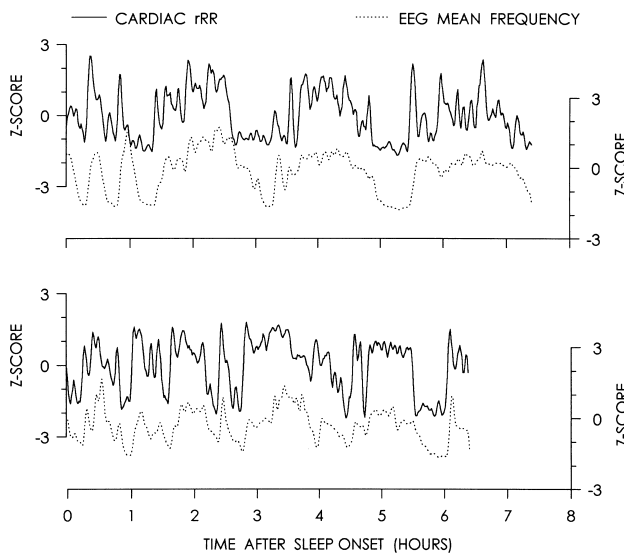


Fig. 3. Concomitant profiles of minute EEG mean frequency and of interbeat autocorrelation coefficient (rRR) after Z-score transformation in two representative subjects during night-sleep. rRR and EEG mean frequency curves were smoothed using the moving average method over a five-point span.

Table 1

Higher cross-correlation coefficients (r) between EEG mean frequency and minute interbeat autocorrelation coefficient (rRR) and RR interval (mean per minute) during sleep periods

| Subjects | N | EEG/rRR | | EEG/RR | |
|----------|-----|---------|----------|--------|----------|
| | | Lag | r | Lag | r |
| 1 | 384 | -1 | +0.610** | -1 | -0.507** |
| 2 | 452 | -1 | +0.267** | +1 | +0.110 |
| 3 | 435 | -2 | +0.453** | -1 | -0.230** |
| 4 | 453 | -1 | +0.286** | -1 | -0.050 |
| 5 | 471 | -1 | +0.367** | -1 | -0.201** |
| 6 | 446 | -1 | +0.497** | -2 | -0.278** |
| 7 | 474 | -1 | +0.465** | +1 | +0.134 |
| 8 | 442 | -1 | +0.592** | -1 | -0.364** |
| 9 | 460 | -1 | +0.216** | -1 | -0.180 |
| 10 | 463 | -2 | +0.353** | -2 | -0.029 |
| 11 | 469 | -2 | +0.638** | 0 | -0.658** |
| 12 | 446 | -2 | +0.554** | -1 | -0.712** |

r was calculated for lags (-10) to (+10), each corresponding to 1 min interval. N is the number of points following sleep onset, each point corresponding to 1 min intervals. For negative lags, heart rate changes anticipate EEG changes, and conversely for positive lags, EEG changes precedes heart rate changes (** $P < 0.001$).

were associated with sleep lightening while decreased rRR coincided with sleep deepening. In contrast, overnight profiles of RR intervals did not show any systematic relationship with EEG activity.

Analysis by rRR gives pertinent information on the moment to moment heart rate variability. An additional concern with the more traditional techniques is the requirement to filter data which have been corrupted by arrhythmic events. In contrast, the cardiac Poincaré plot method can be used on the entire unfiltered data and gives patterns which may be otherwise unrecognised. The higher values of rRR observed during REM sleep compared to NREM sleep mean that the RR intervals are highly regulated during REM sleep despite increased overall variations. In contrast, NREM sleep is accompanied by lower rRR with less coordinated and smaller interbeat variations. However, to describe the sleep EEG as a series of discrete stages can be misleading, because it tends to obscure the fact that sleep is a continuous, oscillatory process [1]. Therefore, we used spectral analysis of the sleep EEG, based on FFT which allows a more detailed description of brain activity than visual sleep stage scoring. Thus, by computing rRR with regard to overnight variations in EEG activity, it appears that heart rate and brain activity are closely linked, the variations in rRR preceding variations in EEG mean frequency by 1–2 min. This corroborates results from Townsend et al. [16] who found that heart rate increases precede spontaneous movements in sleep.

It is recognized that most of the beat to beat variability of heart rate can be attributed to changes in discharge activities of the vagal and sympathetic nerves. Authors using spectral analysis on RR intervals reported that the power spectrum contains both low and high frequency peaks [2,4,10]. Using

appropriate drugs and experimental strategies, they demonstrated that these peaks respectively reflect sympathetic and parasympathetic activity. In recent studies, it has been demonstrated that the Poincaré plots of RR intervals reflect changes of autonomic activity and some indices such as the root mean squared successive difference of RR intervals [3] or the width of Poincaré plot patterns [8] have been proposed as measures of parasympathetic activity. Further investigations will be done in order to clearly establish the importance of rRR as a tool to explore the sympathetic–parasympathetic balance in both physiological and pathological conditions.

In conclusion, this study provides a detailed characterisation of continuous changes in heart rate variability preceding variations in sleep EEG activity, with larger but more regulated interbeat variations when sleep becomes lighter and, conversely, with smaller and less coordinated interbeat variations when sleep becomes deeper. This complex beat to beat behaviour during sleep could not be detected by traditional measures of heart rate variability.

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