Relationship between electroencephalogram slow-wave magnitude and heart rate variability during sleep in humans

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Abstract

To explore whether depth of sleep is related to changes in autonomic control, continuous power-spectral analysis of the electroencephalogram (EEG) and heart rate variability (HRV) was performed in ten normal subjects during nocturnal sleep. Quiet sleep (QS) was associated with an increase in high-frequency power (HF) of HRV (0.15–0.4 Hz) but a decrease in low-frequency power (LF) (0.04–0.15 Hz) to HF ratio (LF/HF) compared with awakening. During QS, LF/HF was significantly and negatively correlated with delta power of EEG (0.5–4.0 Hz), whereas mean R–R interval and HF were not. We conclude that during QS, cardiac sympathetic regulation is negatively related to the depth of sleep, although vagal regulation is not. Our methodology offers a quantitative analysis to study the interaction between cerebral cortical and autonomic functions. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

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Sleep triggers a series of changes in autonomic functions. Previous studies have revealed that quiet sleep (QS) is associated with an increase in vagal function and a decrease in sympathetic function. Such alterations are dramatically reversed in the rapid eye movement (REM) stage [1,12]. Recent advances in the frequency-domain technique of heart rate analysis have presented an opportunity to study cardiac autonomic regulation. For example, it has been generally agreed that high-frequency power (HF) of heart rate variability (HRV) may represent vagal regulation, whereas the low-frequency power (LF) to HF ratio (LF/HF) is related to sympathetic regulation of heart rate [9]. Such a technique is also a valuable tool to study sleep-related autonomic neuroscience. Since sleep ultimately consumes an important fraction of a person’s life, studying changes in autonomic functions during sleep has gradually assumed more importance [9]. With regard to the relationship between depth of QS and autonomic indices, however, it is still being debated whether deeper sleep coincides with a more-augmented vagal tone or with a further attenuation of sympathetic tone as compared with lighter sleep [1,2,10,12].

Slow waves (delta waves) of the electroencephalogram (EEG) are a characteristic of QS. The incidence and amplitude of slow waves have been correlated with the depth of QS; thus traditionally they have been used to define deep (stages 3 and 4) sleep [6]. Although not easily identified in light (stages 1 and 2) sleep from polygraphic tracings, slow waves can still be quantified by power-spectral analysis. After a review of the literature, we were surprised to note that there are still no data on the relationship between slow-wave magnitude and HRV. This lack may be due to the disparities in the classical analytical techniques of the two different physiological signals. The sleep EEG is always reviewed manually in 10-s polysomnographic tracings [6]. On the other hand, 5 min of heart rate data is recommended to perform a ‘short-term’ HRV analysis [9]. In this study, we wanted to develop a new methodology in order to answer such a simple question as whether the HRV indices are related to the slow-wave magnitude during QS. Such a
quantitative description is in fact fundamental to exploring sleep-related alterations in cardiac autonomic controls.

Ten healthy subjects (women/men = 7/3, aged $27.8 \pm 6.3$ year) participated in this investigation. Subjects were volunteer recruits from a university student population and the general public. All were in good health with regular sleep/wake patterns. There was no evidence of hypnotic drug abuse or above-average alcohol, caffeine, or nicotine consumption. None had a past history or current symptoms of psychopathology, or any medical condition known to influence sleep or the autonomic nervous system (ANS). Informed written consent was obtained from all participants, and the experiment protocol was approved by the Ethics Committee of Tzu-Chi Buddhist General Hospital.

EEG (C3/Fz), electro-oculogram (EOG), submental electromyogram (EMG), and electrocardiogram (ECG) were synchronously digitized (at 128 Hz) and stored on a memory card throughout the night via an ambulatory recorder (Micromed MS40P, Italy). Digital signal processing of the physiological signals was performed on an IBM PC-compatible computer. The computer program was written in Pascal (Borland Pascal 7.0, Borland). Preprocessing of the ECG signals was designed according to the recommended procedure [9] and was detailed in our previous investigations [4,11]. In brief, the computer algorithm identified each QRS complex and rejected each ventricular premature complex or noise according to its likelihood in a standard QRS template. The stationary R–R intervals (RR) were resampled and interpolated at the rate of 64 Hz to provide continuity in the time domain. The sampling rate of EEG signals was also reduced to 64 Hz by a bunching algorithm.

The EEG and RR signals to be analyzed were truncated into successive 64-s (4096 points) time segments (windows or epochs) with 50% overlapping. For each time segment, a Hamming window was applied to attenuate the leakage effect [3]. Our algorithm then estimated the power density of the spectral components based on fast Fourier transform. The resulting power spectrum was corrected for attenuation

![Fig. 1. Continuous and simultaneous analysis of polysomnogram and HRV during sleep. EEG and three-dimensional power spectrogram showing successive power-spectral density of the EEG (EPSD) were displayed. Also shown are temporal alterations in the integrated values for the delta power of the spectra. The EOG, EMG, RR, the corresponding three-dimensional power spectrogram of RR (HPSD), and quantified values of the HF and LF powers of the spectra, as well as the LF/HF ratio were likewise monitored.](image-url)
resulting from sampling and the Hamming window [4], and was displayed in gray scale. Each component of the spectrogram was subsequently quantified by the method of integration.

LF (0.04–0.15 Hz), HF (0.15–0.4 Hz), LF/HF of the RR spectrogram, and delta power (0.5–4.0 Hz) of the EEG spectrogram were quantified. They were logarithmically transformed to correct for the skewness of the distribution [4]. Differences among active wakening (AW), QS, and REM were compared using one-way analysis of variance followed by the Student–Newman–Keuls test. Statistical significance was assumed for \( P < 0.05 \). Values are expressed as the means ± SD.

Cyclic changes in EEG spectra were noted during sleep (Fig. 1). The gradual emergence of delta power, either in the spectra or the quantified channel, along with each episode of QS was especially noteworthy. QS also coincided with a significant increase in mean RR and HF but a decrease in LF/HF as compared with an AW state (Table 1). Such alterations were reversed in the REM stage.

Linear regression analysis revealed that the value of LF/HF was negatively correlated with the magnitude of the delta power during QS (Fig. 2). Its correlation coefficient significantly differed from zero (Table 1). This correlation, however, collapsed in AW and REM. By contrast, HF was not significantly correlated with delta power (Fig. 2). Its correlation coefficient could not be discriminated from zero in either AW, QS, or REM (Table 1). Mean RR was not correlated with delta power.

Our data indicate that although QS coincided with an increase in cardiac vagal regulation, the depth of sleep did not have a significant effect on this autonomic index. By contrast, deeper sleep was accompanied by a further suppression of the sympathetic index. Such an observation implies that if one wants to increase his/her vagal tone, a short nap may be sufficient. However, the most pronounced inhibition of sympathetic tone can not be reached unless one enters the deepest sleep. Abnormal representations of autonomic functions during sleep have been suspected of being the etiology of various chronic diseases including essential hypertension [5,8]. The findings of this study may provide some ideas for further investigation.

Frequency-domain analysis of HRV provides a unique aspect of autonomic neuroscience. The standards of measurement, physiological interpretations, and clinical uses of HRV were reported in 1996 [9]. HF indicates vagal modulations on cardiac pacemaker whereas LF/HF reflects sympathetic modulations or sympathovagal balance. In that report, developments of HRV measurements such as automatic and multisignal analysis, as well as more-involved research of HRV during sleep were given as future possibilities [9]. We have developed a computer algorithm for automatic HRV analysis to study the effects of gender and aging on HRV in a large population [4]. This algorithm was modified for this study to achieve an automatic, continuous, and multisignal analysis in order to meet the needs of a sleep study. Vigorous changes of HRV during different stages of sleep can be vividly demonstrated with this technique (Fig. 1).

Cyclic changes in heart rate during sleep have been noted for a long time. It has been generally agreed that QS is accompanied by more vagal activity but less sympathetic

### Table 1

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<th>AW</th>
<th>QS</th>
<th>REM</th>
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<tr>
<td>RR (ms)</td>
<td></td>
<td></td>
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<tr>
<td>Mean</td>
<td>848 ± 114</td>
<td>1044 ± 119&lt;sup&gt;c&lt;/sup&gt;</td>
<td>885 ± 140</td>
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<tr>
<td>( r )</td>
<td>-0.23 ± 0.26</td>
<td>0.08 ± 0.27&lt;sup&gt;c&lt;/sup&gt;</td>
<td>-0.28 ± 0.36</td>
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<tr>
<td>HF (ln(ms&lt;sup&gt;2&lt;/sup&gt;))</td>
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<tr>
<td>Mean</td>
<td>5.77 ± 0.56</td>
<td>6.50 ± 0.65&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5.58 ± 0.97</td>
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<tr>
<td>( r )</td>
<td>0.00 ± 0.25</td>
<td>0.03 ± 0.22</td>
<td>0.01 ± 0.30</td>
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<tr>
<td>LF/HF (ln(ratio))</td>
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<tr>
<td>Mean</td>
<td>1.50 ± 0.39</td>
<td>0.27 ± 0.59&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.22 ± 0.53</td>
</tr>
<tr>
<td>( r )</td>
<td>0.27 ± 0.18</td>
<td>-0.33 ± 0.08&lt;sup&gt;c,d&lt;/sup&gt;</td>
<td>0.20 ± 0.28</td>
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<sup>a</sup> Results are expressed as means ± SD.
<sup>b</sup> AW, active wakening; QS, quiet sleep; REM, rapid eye movement sleep; RR, R–R intervals; HF, high-frequency power; LF/HF, low-frequency power to HF ratio; \( r \), correlation coefficient with delta power of EEG.
<sup>c</sup> \( P < 0.05 \); significantly different from AW.
<sup>d</sup> \( P < 0.05 \); significantly different from zero value, for \( r \) only.

Fig. 2. Two-dimensional scattergram showing the relation between delta power and corresponding HF, LF/HF ratio of HRV of one subject during QS.
activity compared with AW and REM [1,12]. Following the staging system of Rechtschaffen and Kales [6], pioneer studies by Zemaityte et al. [12] showed that the increase in sleep stage coincides with a gradual decrease or increase in vagal function in subjects with initially high or moderate parasympathetic tones, respectively. They also described that the sympathetic input remains relatively constant throughout all stages of sleep, except for its decrease during stage 1. In another study, the largest parasympathetic influence was observed in stage 2 [10]. Reports by Baharav et al. [1] and Bonnet and Arand [2], however, demonstrated that HF persistently increases even in the deep sleep stages, and behaves as a mirror image of LF and LF/HF. Such discrepancies have been attributed to differences in the analytical window length and strategies of sleep staging [2], even though all research groups followed the same staging principles defined by Rechtschaffen and Kales.

From a technical view, the traditional sleep staging method uses 10-s polygraphic tracings to determine a stage score [6]. Regarding the analysis of HRV, it has been suggested to use 5-min ECG signals to perform a ‘short-term’ HRV analysis [9]. The great disparity in analysis window length between polysomnographic and HRV analyses has led to serious barriers in sleep-related autonomic research. A longer time window may have a smear effect on the EEG analysis especially when sleep is changing from one stage to another. On the other hand, too short a window can not detect slow HRVs such as LF. Thus, we made a compromise in window length to cover both EEG and HRV analyses. Using a fixed 64-s time window, a worse yet acceptable temporal resolution was obtained for EEG, while the corresponding frequency resolution (0.016 Hz) was enough to detect LF of HRV (0.04–0.15 Hz). More importantly, a single time window length can provide ideal synchronization of the two signals. We have tried shorter (32-s) and longer (128-s) time windows, and obtained similar results as with a 64-s time window. Under such conditions, we found that the dependencies of the two autonomic indices on the delta wave magnitude definitely differ. LF/HF is negatively dependent on the delta power, whereas HF is independent of it. The correlation analysis between delta power and the HRV indices may provide an alternative insight into the interplay between the ANS and the cerebral cortex.

Sleep-related autonomic neuroscience has recently increased in popularity. Some interesting findings and hypotheses have been reported. For example, the ANS function exhibits a specific pattern in obstructive sleep apnea patients [7]. A hyperactive sympathetic function during sleep is suspected to be the etiology of some proportion of essential hypertension [8]. The majority of previous studies were based on the staging principle of Rechtschaffen and Kales. Others, however, did not even stage QS which may be due, at least partly, to the complexity and parametric nature of the traditional staging system. Nevertheless, our methodology offers a simple and quantitative analysis to study the interaction between cerebral cortical and autonomic functions without using specific terminology of different waveforms in conventional sleep staging. It is especially suitable for analyzing autonomic dynamics during QS. We hope that such views will be useful in future applications.

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