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Spectral Analysis of Heart Rate Variability in Sleep

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Summary

Spectral analysis of heart rate variability (HRV) during overnight polygraphic recording was performed in 11 healthy subjects. The total spectrum power, power of the VLF, LF and HF spectral bands and the mean R-R were evaluated. Compared to Stage 2 and Stage 4 non-REM sleep, the total spectrum power was significantly higher in REM sleep and its value gradually increased in the course of each REM cycle. The value of the VLF component (reflects slow regulatory mechanisms, e.g. the renin-angiotensin system, thermoregulation) was significantly higher in REM sleep than in Stage 2 and Stage 4 of non-REM sleep. The LF spectral component (linked to the sympathetic modulation) was significantly higher in REM sleep than in Stage 2 and Stage 4 non-REM sleep. On the contrary, a power of the HF spectral band (related to parasympathetic activity) was significantly higher in Stage 2 and Stage 4 non-REM than in REM sleep. The LF/HF ratio, which reflects the sympathovagal balance, had its maximal value during REM sleep and a minimal value in synchronous sleep. The LF/HF ratio significantly increased during 5-min segments of Stage 2 non-REM sleep immediately preceding REM sleep compared to 5-min segments of Stage 2 non-REM sleep preceding the slow-wave sleep. This expresses the sympathovagal shift to sympathetic predominance occurring before the onset of REM sleep. A significant lengthening of the R-R interval during subsequent cycles of Stage 2 non-REM sleep was documented, which is probably related to the shift of sympathovagal balance to a prevailing parasympathetic influence in the course of sleep. This finding corresponds to a trend of a gradual decrease of the LF/HF ratio in subsequent cycles of Stage 2 non-REM sleep.

Key words

Autonomic nervous system • Cardiac activity • Heart rate variability • Orexin • Sleep

Introduction

Many autonomic and endocrine changes in the course of sleep have been described repeatedly (Gronfier and Brandenberger 1998, Dauvilliers 2003). Some of them stay under control of the circadian rhythmicity, others are influenced by the sleep *per se* or by both processes. There are prominent changes of heart rate during sleep, with its decrease of 5-10 % in the non-REM sleep (mostly 55-60 beats per minute) compared to the values during the wakefulness and with a further decrease in the course of the night (Snyder *et al.* 1964, Coccagna a Scaglione 2003). During the REM sleep an increase of the heart rate with the maximal values accompanying the

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onset of the ponto-geniculo-occipital activity was registered (Dauvilliers 2003). The blood pressure decreases during non-REM sleep to 77-80 % of its values during wakefulness (Coccagna *et al.* 2003). In the REM sleep the values of blood pressure are similar as in Stage 2 non-REM with an increase during ponto-geniculo-occipital activity (Coccagna and Scaglione 2003, Dauvilliers 2003). In the digestive system, reduced production of saliva, decreased contractions of the upper esophageal sphincter, and reduced peristaltic activity of the lower esophagus, duodenum and gut both during non-REM and REM sleep have been described (Castiglione *et al.* 1993, Benoit and Goldenberg 1997).

Autonomic activity during sleep has been evaluated in several studies using spectral analysis of the heart rate variability (Vaughn *et al.* 1995, Baharav *et al.* 1995, Scholz *et al.* 1997, Elsenbruch *et al.* 1999). The parameters derived from the spectral analysis of HRV include a very low frequency (VLF) spectral component (0.003-0.05 Hz) which is possibly related to long-term regulatory mechanisms (e.g. the renin-angiotensin system, the thermoregulatory peripheral blood flow adjustment); the low frequency (LF) spectral component (0.05-0.15 Hz) which is linked to sympathetic modulation, but also includes some parasympathetic influence; and the high frequency (HF) spectral band (0.15-0.4 Hz) which reflects parasympathetic (vagal) activity (Saul *et al.* 1990, Malliani *et al.* 1991, Montano *et al.* 1994, Task Force 1996, Pagani *et al.* 1997, Ewing 1999). During sleep, a decrease of the LF component was registered in Stage 2 non-REM and more prominently in Stage 4 non-REM sleep. On the contrary, an increase of the LF component was documented in REM sleep. The power of the HF spectral band was converse to the changes of the LF component, with a reduction in the REM and with an increase in the non-REM sleep (Vaughn *et al.* 1995, Baharav *et al.* 1995). Some studies have described a decrease of the power in all spectral bands during non-REM sleep (Vaughn *et al.* 1995, Bonnet and Arand 1997). Ferini-Strambi *et al.* (2000) have studied the influence of a cyclic alternating pattern (CAP) on the spectral analysis of HRV and found an elevated value of the LF component and of the LF/HF ratio and a reduction in the HF spectral band during the CAP-phase both in Stage 2 and 4 non-REM sleep.

In our study, we evaluated the power in the LF and HF spectral bands and the changes of the VLF spectral band and the total spectrum power in individual sleep stages, in individual sleep cycles and in different segments of each sleep stage. The effect of transition from Stage 2 non-REM sleep either to slow wave sleep or to REM sleep on the parameters of the spectral analysis of HRV was also assessed.

Methods

In our study, 11 healthy volunteers (6 females and 5 males) 29.6±10.6 years-old (range 12-52 years) underwent two standard overnight polygraphic recordings and only the data from the second night were included in this study. The first overnight polygraphic recording excluded any sleep disorder such as sleep apnea syndrome or periodic leg movements. The polygraphic recordings were made using the standard placement of the EEG electrodes (F4-C4, C4-P4, F3-C3, C3-P3, C4-A1 and C3-A2, sampling rate 128 Hz), the sub-mental and bilateral anterior tibialis EMG, the horizontal electrooculogram, a thermistor for the recording of respiration and the infra red video camera. Polysomnography was started between 22:00 to 23:00 h and was terminated by spontaneous awakening between 06:00 and 08:00 h.

In the course of polygraphic recordings the heart rate signal was obtained from a surface pre-cordial ECG lead (sampling rate 500 Hz), the R-R interval sequence was obtained by a computerized algorithm of ECG registration. The calculation of the time series trend was assessed and a non-equidistant time sequence was interpolated with the help of a third grade function – cubic spline – and further sampled at a sampling frequency of 4 Hz. Fast Fourier transformation of the adjusted time series was then carried out to determine the power spectral analysis which was decomposed into the following spectral components: VLF 0.02-0.05 Hz, LF 0.05-0.15 Hz and HF 0.15-0.4 Hz. The analysis was performed at repeated ectopic-free intervals of approximately 5 min (256 beats) during (1) 15-20 min of the awake state before falling a sleep (when the lights were on and wakefulness was controlled by a technician and the EEG), during (2) Stage 2 non-REM sleep, (3) Stage 4 non-REM sleep and (4) REM sleep. In this way the whole course of the mentioned sleep stages was analyzed eliminating only the segments containing ectopic beats, movement artifacts or arousals.

The following parameters were evaluated: the mean R-R intervals, the power of the VLF (we only registered a part of the VLF spectral band corresponding to the short-term recording), LF and HF components,

total spectrum power, relative value of the VLF component (= the power of this component divided by the total spectrum power), the normalized spectral power of the LF and HF spectral bands (= ratio between the power of these components and the total spectrum power minus the power in the VLF band) and the LF/HF ratio which reflects the sympathovagal balance (Malliani *et al.* 1996). The examination was performed 24 hours after the subjects had avoided any violent or moderate physical exercise, with the last light meal 3 or more hours before the examination, after 8 hours without smoking, tea, coffee and alcohol deprivation, and in subjects without any acute health problems, physical or psychical discomfort. All subjects with any diseases known to affect autonomic functions, such as alcoholism or diabetes, patients with cardiac diseases or receiving medication which may have affected the HRV (e.g. antihypertensive drugs, antiarrhythmics, anticholinergic drugs or tricyclic antidepressants) were excluded. Furthermore, women were excluded during the premenstrual and menstrual period.

Statistical analysis included the analysis of variance (ANOVA), the Friedman test, the Tukey test (for post-hoc multiple comparison), Student´s t-test, and the Wilcoxon matched paired test. The normal distribution was evaluated by using the D´Agostino Omnibus test and the Shapiro-Wilks test. A value of $P<0.05$ was considered significant.

Results

The macrostructural polygraphic parameters are shown in Table 1.

The spectral analysis of HRV in individual sleep stages

Individual sleep stages differed in the total spectrum power (df=3, χ^2=14.9; $P<0.01$), its value being significantly higher in REM than in Stage 4 ($P<0.01$) and Stage 2 non-REM sleep ($P<0.01$). The values of the total spectrum power and of its individual spectral bands in absolute values are shown in Table 2.

Table 1. Polygraphic macrostructural parameters (n=11).

Total Sleep Time (min)	425.6 ± 73.4
Number of Sleep Cycles	4.27 ± 0.96
Sleep Efficiency (%)	91.9 ± 3.0
Sleep Onset Latency (min)	18.0 ± 14.5
Stage 1 non-REM (%)	3.0 ± 1.3
Stage 2 non-REM (%)	41.0 ± 6.2
Stage 3 non-REM (%)	6.8 ± 1.5
Stage 4 non-REM (%)	20.7 ± 4.7
REM (%)	23.4 ± 2.6
Wakefulness (%)	5.4 ± 2.2

The changes of the total spectrum power between different sleep stages also influenced the absolute value of its spectral components. In order to eliminate this effect of total spectrum power fluctuations between different sleep stages, only the relative or normalized value of individual spectral components and the LF/HF ratio were assessed. The relative values of the VLF band in the short-term recordings differed between individual sleep stages (df=3; F=3.38; $P<0.05$) with the highest value in REM sleep as is obvious from Table 3. This observation means that a redistribution of the total power into the VLF spectral band occurred during REM sleep.

The LF component differed significantly in normalized units between individual sleep stages (df=3; F=5.01; $P<0.01$), the highest value being observed in REM sleep, as shown in Table 3.

Table 2. The total spectrum power and its individual components in absolute values in different sleep stages (n=11).

	Wakefulness	**Stage 2 non-REM**	**Stage 4 non-REM**	**REM sleep**
Total Power (ms^2)	2267 ± 2068	3611 ± 3318**	2747 ± 3197**	4028 ± 3746
VLF (ms^2)	372 ± 333	364 ± 247	299 ± 261	733 ± 516
LF (ms^2)	747 ± 693	970 ± 571	671 ± 538	1222 ± 798
HF (ms^2)	1148 ± 1148	2277 ± 2878	1777 ± 2789	2073 ± 3158

**P<0.01 (difference from REM sleep)

Table 3. Spectral analysis of the HRV in different sleep stages (n=11).

	Wakefulness	Stage 2 non-REM	Stage 4 non-REM	REM sleep
LF/HF	1.03 ± 0.9**	1.07 ± 0.82**	0.98 ± 0.79**	2.40 ± 1.96
REL.VLF (%)	18.6 ± 9.9	16.2 ± 9.2*	16.2 ± 6.5*	26.0 ± 13.8
LF (n.u.)	0.43 ± 0.16	0.42 ± 0.17*	0.40 ± 0.18**	0.55 ± 0.21
HF (n.u.)	0.57 ± 0.16	0.58 ± 0.17*	0.60 ± 0.18**	0.45 ± 0.21

REL.VLF = the power of the VLF spectral band divided by the total power; LF (n.u.), HF (n.u.) – the LF and HF component in normalized units = the power of these components divided by the total power minus the VLF band; *P<0.05, **P<0.01 (difference from REM sleep)

The HF component differed between individual sleep stages (df=3; F=4.99;P<0.01). The value of this spectral band was in a reciprocal relation to the aforementioned LF component and its value was higher in Stage 4 non-REM and in Stage 2 non-REM sleep than in REM sleep. The values of the HF component in normalized units are depicted in Table 3. The reciprocal changes of the LF and the HF components in the synchronous and the REM sleep are also reflected by the LF/HF ratio which is different in individual sleep stages (df=3; χ^2=11.4; P<0.01) with the lowest value in Stage 4 non-REM and the highest value in REM sleep. For details see Table 3.

A detailed analysis of Stage 2 non-REM sleep

Comparing the segments of Stage 2 non-REM sleep (which were between REM and slow-wave sleep) and the segments of Stage 2 non-REM sleep (which were between slow-wave sleep and REM), no differences were revealed. The initial 5-minute, the final 5-minute and the remaining medial segment of each cycle of Stage 2 non-REM sleep also did not differ in any parameter of the spectral analysis of HRV. A statistically significant difference in the LF/HF ratio was found when the 5-minute final segment immediately preceding the REM sleep with the 5-minute segment preceding the slow-wave sleep were compared (Z=2.1; P<0.05) with a higher value of the LF/HF ratio in Stage 2 non-REM before REM (=1.61±1.28) than before slow-wave sleep (=0.96 ±1.28).

Individual cycles of Stage 2 non-REM sleep differed significantly in the LF/HF ratio (df=3; χ^2=8.5; P<0.05), but in the *post hoc* multiple comparison of the individual cycles there was only a trend of the LF/HF ratio to higher values in the first than in the third (P=0.05) and than in the fourth cycle (P<0.6). In the 1st cycle the LH/HF ratio was 1.69 ±1.84, in the 2nd cycle 1.48 ±1.46, in the 3rd cycle 0.89±0.53 and in the 4th cycle 0.99±0.83.

A detailed analysis of Stage 4 non-REM sleep

Comparing individual cycles of Stage 4 non-REM sleep and comparing initial, medial and final segments in each cycle no differences were found in the parameters of spectral analysis of the HRV.

A detailed analysis of REM sleep

No difference was found between individual cycles of REM sleep. A significant increase of the total spectrum power in the course of each cycle of REM sleep was observed (df=2; χ^2=13.4; P=0.001). The total spectrum power was significantly lower in the initial 5-minute segment (= 2917±3404 ms^2) than in the last 5-minute segment (= 4762±5120 ms^2) (P=0.01) and than in the remaining medial segment (= 3899±3357 ms^2) (P<0.01). No changes of the proportion of the individual spectral bands or of the LF/HF ratio were found in the course of REM cycles.

R-R mean values

Significant differences of R-R were observed between individual sleep stages (df=3; F=7.77; P<0.001), the R-R interval being significantly longer in synchronous sleep compared to wakefulness. See Table 4.

Table 4. The RR-mean in different sleep stages (n=11).

	RR mean (ms)
Wakefulness	0.943 ± 0.142
Stage 2 non-REM	1.061 ± 0.155***
Stage 4 non-REM	1.035 ± 0.157 **
REM sleep	1.006 ± 0.153

**P<0.01, ***P<0.001 (difference from wakefulness)

There was statistically significant lengthening of the R-R interval in the course of sleep when the individual cycles of Stage 2 non-REM sleep were compared (df=3; F=4.98, P<0.01), the R-R interval being significantly longer in the 4th cycle (P=0.01) and in the 3rd cycle (P<0.05) compared to the 1st one. A gradual lengthening of the R-R interval was also observed in subsequent cycles of Stage 4 non-REM and in REM sleep, however, these differences did not reach statistical significance. The R-R mean in the course of sleep is depicted in Figure 1.

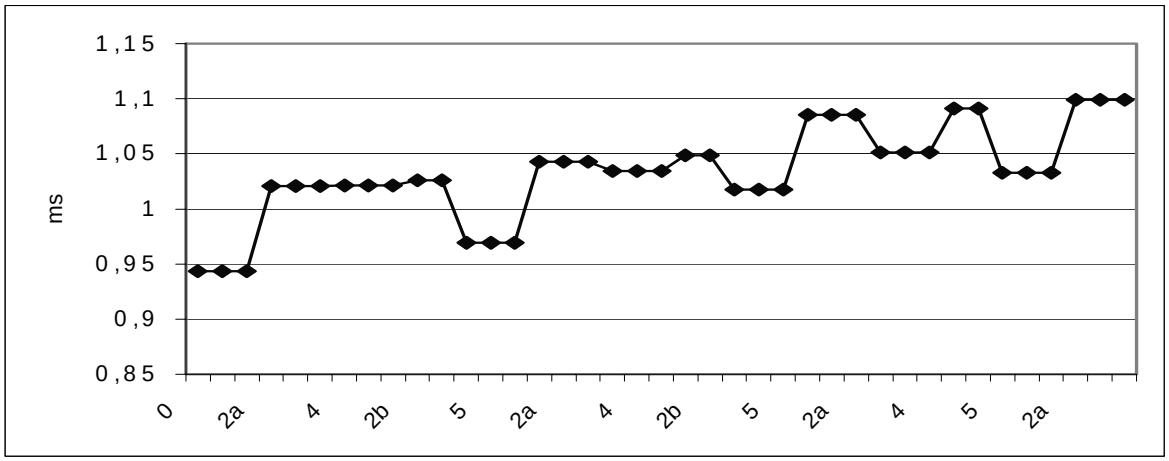

Fig. 1. R-R mean (averaged values from all 11 subjects) in the course of sleep. 0=wakefulness, 2a=Stage 2 non-REM between REM and Stage 4 non-REM, 2b=Stage 2 non-REM between Stage 4 non-REM and REM, 4=Stage 4 non-REM, 5=REM sleep.

Discussion

In our study, significant changes in the parameters of spectral analysis of HRV were followed in the course of sleep. The value of total spectrum power culminated during REM sleep and had the lowest value in wakefulness and in Stage 4 non-REM sleep. Fluctuations of the total power between different sleep stages had a prominent impact on the absolute values of the power in the VLF, LF and HF spectral bands; it was thus necessary to assess the relative or normalized value of these components to eliminate the effect of total power changes. An assessed part of the VLF spectral band in short-term recordings had lower absolute and relative values in synchronous sleep with their minimum in Stage 4 non-REM sleep. On the contrary, during REM sleep an increase of both absolute and relative power was found in this spectral band. Taking into account the fact that the VLF component reflects slow regulatory mechanisms such as the renin-angiotensin system and thermoregulatory processes, it may be concluded that those regulatory mechanisms are more active during REM sleep and that they cease during slow-wave sleep.

The highest normalized value of the LF component was found in REM sleep, meanwhile a decrease of this spectral band was registered in synchronous sleep with a minimal value in Stage 4 non-REM sleep. This spectral component in the supine position is mediated both by sympathetic and parasympathetic activity and its elevation with a concomitant reduction of the HF component (see further) in REM sleep means that the sympathetic activity in this sleep stage is increased.

The HF spectral band had the lowest normalized value in REM sleep. On the contrary, during synchronous sleep an elevation of this component in normalized units was registered. Due to the fact that the HF component originates from the respiration-related vagal activity, it may be estimated that the parasympathetic activity is reduced and sympathetic activity increased in REM sleep and *vice versa* in synchronous sleep. The changes in the sympathovagal balance during different sleep stages are also reflected by the LF/HF ratio, the lowest value of which was found in Stage 4 of non-REM sleep and conversely the highest value in REM sleep. The described changes of the LF and HF components and of the sympathovagal balance during REM and non-REM sleep correspond to the results of other studies (Vaughn *et al.* 1995, Baharav *et al.* 1995, Scholz *et al.* 1997, Bonnet and Arand 1997). The sympathetic activation reflected by an elevation of the LF spectral band is in accordance with the finding of an increase of activity registered directly

from sympathetic fibers by a microneurographic technique during REM sleep in some previous studies (Okada *et al.* 1991, Somers *et al.* 1993).

It was interesting that the sympathovagal shift to sympathetic predominance (reflected as an increase in the value of the LH/HF ratio) already occurred during Stage 2 of non-REM sleep before the onset of REM sleep. A similar finding was also observed by other authors (Bonnet and Arand 1997, Scholz *et al.* 1997). This means that the autonomic changes precede changes of the sleep stage. Apart from the sympathovagal shift to prevailing sympathetic modulation of the cardiac activity during REM sleep, an increase of the total spectrum power at this sleep stage was revealed and is probably brought about by an activation in both branches of the autonomic nervous system (sympathetic and parasympathetic). The increase of total power during each REM cycle was gradual with the highest value at the end of each REM cycle.

In the course of sleep, a progressive lengthening of the R-R interval was registered with superposition of the oscillation of the R-R mean during different sleep stages. This gradual lengthening of R-R interval probably originates from a progressive shift of the sympathovagal balance to a prevailing vagal influence in the course of sleep and is connected with a regeneration of the organism during sleep. The trend of a gradual reduction of the LF/HF ratio in the course of subsequent cycles of Stage 2 non-REM sleep observed in our study corresponds with this finding.

Activation of the autonomic nervous system with the sympathovagal shift to the prevailing sympathetic activity during REM sleep may be conditioned by several mechanisms occurring during this sleep stage. During REM sleep an activation of orexinergic neurons has been described in the perifornical region of the hypothalamus (Kilduff and Peyron 2000, Alam *et al.* 2002). The orexinergic projections not only exert an effect on the sleep-wake cycle, but they also influence the structures which participate in the regulation of the autonomic nervous system, such as the periaqueductal grey, the paraventricular hypothalamic nucleus, the ventrolateral medullar tegmentum, the noradrenergic group A5, the parabrachial reticular formation, the area postrema, the nucleus of the solitary tract, the dorsal vagal nucleus, the rapheal nuclei, the insular and the infralimbic cortex (Peyron *et al.* 1998, Date *et al.* 1999, Salin-Pasqual *et al.* 2001, Shirasaka *et al.* 2002, Llewellyn-Smith *et al.* 2003). An important role of the orexinergic system in the regulation of the autonomic system was documented by the experiments, in which electrical stimulation of the perifornical hypothalamic region elevated the blood pressure and heart rate. Similarly, intraventricular application of orexin increases the heart rate, blood pressure and activity of the renal sympathetic fibers (Samson *et al.* 1999).

The activation of central motor and limbic structures in dreaming could also be responsible for the increase of sympathetic activity during REM sleep (Smith *et al.* 1990, Stickgold *et al.* 2001, Siegel 2001, Kaufmann *et al.* 2002). This hypothesis is in accordance with the observation that phasic activation of the autonomic nervous system with an increase of heart rate and blood pressure accompanies ponto-geniculo-occipital activity which is characterized by phasic activation of the dreaming process with an increase of its visual vividness and with enhanced emotionality (Hobson 1990, Kahn *et al.* 1997, Adrien 2003, Dauvilliers 2003, Coccagna and Scaglione 2003).

The aforementioned changes of autonomic activity during sleep are also responsible for the alterations of cardiac activity under physiological and pathophysiological situations. Thus, during non-REM sleep sinus bradycardia (less than 40 bpm), sinus pauses longer than 1.75 s or transient atrioventricular block, can be frequently observed mostly in young healthy men (Brodsky *et al.* 1977, Otsuka *et al.* 1983). Sometimes, supraventricular arrhythmias (mostly ectopic beats or tachycardia) and less frequently ventricular tachycardias occur in sleep; mostly in older subjects and predominantly in relation to REM sleep or sleep-wake transitions (Smith *et al.* 1972, Rosenblatt *et al.* 1973, Adlakha and Shepard 1998). An increase of vagal modulation of cardiac activity and a decrease of the sympathetic influence during the non-REM sleep result in the reduction of heart rate, augmentation of the myocardial refractory phase and in a reduction of conductivity of the atrioventricular node. On the contrary, increased activity of the cardiac sympathetic fibers in the REM sleep facilitates the myocardial depolarization, shortens the refractory phase, elevates the heart rate and reduces the fibrillatory threshold (Somers *et al.* 1993, Adlakha and Shepard 1998).

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References

ADLAKHA A, SHEPARD JW: Cardiac arrhythmias during normal sleep and in the obstructive sleep apnea syndrome. *Sleep Med Rev* **2:** 45-60, 1998.

ADRIEN J: Neurobiology of the sleep-wake cycle. In*: Sleep. Physiology, Investigations, and Medicine*. M BILLIARD (ed), Kluwer Academic/Plenum Publishers, New York, 2003, pp 31-43.

ALAM MN, GONG H, ALAM T, JAGANATH R, MCGINTY D, SZYMUSIAK R: Sleep-waking discharge patterns of neurons recorded in the rat perifornical lateral hypothalamic area. *J Physiol Lond* **538:** 619-631, 2002.

BAHARAV A, KOTAGAL S, GIBBONS V, RUBIN BK, PRATT G, KARIN J, AKSELROD S: Fluctuations in autonomic nervous activity during sleep displayed by power spectrum analysis of heart rate variability. *Neurology* **45:** 1183-1187, 1995.

BENOIT O, GOLDENBERG F: Exploration du sommeil et de la vigilance chez l´adulte. *Éditions médicales internationales*, Allée de la Croix-Bossée, 1997.

BONNET MH, ARAND DL: Heart rate variability: sleep stage, time of night, and arousal influences. *Electroenceph Clin Neurophysiol* **102**: 390-396, 1997.

BRODSKY M, WU D, DENES P, KANAKIS C, ROSEN KM: Arrhythmias documented by 24-hour continuous electrocardiographic monitoring in 50 male medical students without apparent heart disease. *Am J Cardiol* **39**: 390-395, 1977.

CASTIGLIONE F, EMDE C, ARMSTRONG D, SCHNEIDER P, BAUERFEIND P, STACHER G, BUM AL: Nocturnal oesophageal motor activity is dependent on sleep stage. *Gut* **34**: 1653-1659, 1993.

COCCAGNA G, SCAGLIONE C: Cardiocirculatory disorders and sleep. In*: Sleep. Physiology, Investigations, and Medicine*. M BILLIARD (ed), Kluwer Academic/Plenum Publishers, New York, 2003, pp 589-597.

DATE Y, UETA Y, YAMASHITA H, YAMAGUCHI H, MATSUKARA S, KANGAWA K, SAKURAI T, YANAGISAWA M, NAKAZATO M: Orexins, orexinergic hypothalamic peptides, interact with autonomic, neuroendocrine and neuroregulatory systems. *Proc Natl Acad Sci USA* **96**: 748-753, 1999.

DAUVILLIERS Y: The major physiological functions during sleep. In*: Sleep. Physiology, Investigations, and Medicine*. M BILLIARD (ed), Kluwer Academic/Plenum Publishers, New York, 2003, pp 45-60.

ELSENBRUCH S, HARNISH MJ, ORR WC: Heart rate variability during waking and sleep in healthy males and females. *Sleep* **22**: 1067-1071, 1999.

EWING DJ: Analysis of heart rate variability and other non-invasive tests with special reference to diabetes mellitus. In: *Autonomic Failure: A Textbook of Clinical Disorders of the Autonomic Nervous System*. R BANNISTER, CJ MATHIAS (eds), Oxford University Press, Oxford, 1999, pp 312-333.

FERINI-STRAMBI L, BIANCHI A, ZUCCONI M, OLDANI A, CASTRONOVO V, SMIRNE S: The impact of cyclic alternating pattern on heart rate variability during sleep in healthy young adults. *Clin Neurophysiol* **111**: 99-101, 2000.

GRONFIER C, BRANDENBERGER G: Ultradian rhythms in pituitary and adrenal hormones: their relations to sleep. *Sleep Med Rev* **2**: 17-29, 1998.

HOBSON JA: Sleep and dreaming. *J Neurosci* **10**: 371-382, 1990.

KAHN D, PACE-SCHOTT EF, HOBSON JA: Consciousness in waking and dreaming: the roles of neuronal oscillation and neuromodulation in determining similarities and differences. *Neuroscience* **78**: 13-38, 1997.

KAUFMANN H, BHATTACHARYA KF, VOUSTIANIOUK A, GRACIES JM: Stimulation of the subthalamic nucleus increases heart rate in patients with Parkinson disease. *Neurology* **59**: 1657-1658, 2002.

KILDUFF TS, PEYRON C: The hypocretin/orexin ligand-receptor system: implications for sleep and sleep disorders. *Trends Neurosci* **23**: 359-365, 2000.

LLEWELLYN-SMITH IJ, MARTIN CL, MARCUS JN, YANAGISAWA M, MINSON JB, SCAMMELL TE: Orexin-immunoreactive inputs to rat sympathetic preganglionic neurons. *Neurosci Lett* **351**: 115-119, 2003.

MALLIANI A, PAGANI M, LOMBARDI F, CERUTTI S: Cardiovascular neural regulation explored in the frequency domain. *Circulation* **84**: 1482-1492, 1991.

MALLIANI A, PAGANI M, LOMBARDI F: Methodological aspects of non-invasive analysis of autonomic regulation of cardiovascular variability. *Clin Sci* **91** (Suppl): 68-71, 1996.

MONTANO A, RUSCONE TG, PORTA A, LOMBARDI F, PAGANI M, MALLIANI A: Power spectrum analysis of heart rate variability to assess the changes in sympathovagal balance during graded orthostatic tilt. *Circulation* **90**: 1826-1831, 1994.

OKADA H, IWASE S, MANO T, SUGIYAMA Y, WATANABE T: Changes in muscle sympathetic nerve activity during sleep in humans. *Neurology* **41**: 1961-1966, 1991.

OTSUKA K, ICHIMARU Y, YANAGA T: Studies of arrhythmias by 24-hour polygraphic recordings: relationship between atrioventricular block and sleep states. *Am Heart J* **105**: 934-940, 1983.

PAGANI M, MONTANO A, PORTA A, MALLIANI A, ABBOUD FM, BIRKETT C, SOMERS VK: Relationship between spectral components of cardiovascular variabilities and direct measures of muscle sympathetic nerve activity in humans. *Circulation* **95**: 1441-1448, 1997.

PEYRON C, TIGHE DK, POL AN, LECEA L, HELLER HC, SUTCLIFFE JG, KILDUFF TS: Neurons containing hypocretin (orexin) project to multiple neuronal systems. *J Neurosci* **18**: 9996-10015, 1998.

ROSENBLATT G, HARTMANN F, ZILLING GR: Cardiac irritability during sleep and dreaming. *J Psychosom Res* **17**: 129-134, 1973.

SALIN-PASQUAL R, GERASHCHENKO D, GRECO MA, BLANCO-CENTURION C, SHIROMANI PJ: Hypothalamic regulation of sleep. *Neuropsychopharmacol* **25**: S21-S27, 2001.

SAMSON WK, GOSNELL B, CHANG JK, RESCH ZT, MURPHY TC: Cardiovascular regulatory actions of the hypocretins in brain. *Brain Res* **831**: 248-253, 1999.

SAUL JP, REA RF, ECKBERG DL, BERGER RD, COHEN J: Heart rate and muscle sympathetic nerve variability during reflex changes of autonomic activity. *Am J Physiol* **258**: H713-H721, 1990.

SCHOLZ UJ, BIANCHI AM, CERUTTI S, KUBICKI S: Vegetative background of sleep: spectral analysis of the heart rate variability. *Physiol Behav* **62**: 1037-1043, 1997.

SHIRASAKA T, KUNITAKE T, TAKASAKI M, KANNAN H: Neuronal effects of orexins: relevant to sympathetic and cardiovascular functions. *Regul Pept* **104**: 91-95, 2002.

SIEGEL JM: The REM sleep-memory consolidation hypothesis. *Science* **294**: 1058-1063, 2001.

SMITH R, JOHNSON L, ROTHFELD D: Sleep and cardiac arrhythmias. *Arch Intern Med* **130**: 751-753, 1972.

SMITH OA, DEVITO JL, ASTLEY CA: Neurons controlling cardiovascular responses to emotion are located in lateral hypothalamus-perifornical region. *Am J Physiol* **259**: R943-R954, 1990.

SNYDER F, HOBSON JA, MORRISON DF, GOLDFRANK F: Changes in respiration, heart rate, and systolic blood pressure in human sleep. *J Appl Physiol* **19**: 417-422, 1964.

SOMERS VK, PHIL D, DYKEN ME, MARK AL, ABBOUD FM: Sympathetic-nerve activity during sleep in normal subjects. *N Engl J Med* **328**: 303-307, 1993.

STICKGOLD R, HOBSON JA, FOSSE R, FOSSE M: Sleep, learning, and dreams: off-line memory reprocessing. *Science* **294**: 1052-1057, 2001.

TASK FORCE OF THE EUROPEAN SOCIETY OF CARDIOLOGY AND THE NORTH AMERICAN SOCIETY OF PACING AND ELECTROPHYSIOLOGY: Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *Circulation* **93**: 1043-1065, 1996.

VAUGHN BV, QUINT SR, MESSENHEIMER JA, ROBERTSON KR: Heart period variability in sleep. *Electroenceph Clin Neurophysiol* **94**: 155-162, 1995.

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