COST ACTION B27 ELECTRIC NEURONAL OSCILLATIONS AND COGNITION
MC and WGs Joint Seminar: Brain Electricity and Cognition
Skopje, 12-13 May 2006

HEART RATE VARIABILITY AS A REFLECTION OF BRAIN FUNCTIONS DURING SLEEP

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Night sleep with the changes of sleep stages might be seen as a natural situation of modifications in central nervous system functional status. Those modifications are followedby the changes in autonomic control of cardiovascular system. Thus, night sleep might be seen as a natural model for investigation of autonomic heart rate (HR) control during sleep. On the other hand, HR modifications during the shifts of sleep stages might be a basis for evaluation of sleep stages as well as new defined sleep states.

Research aims in the framework of COST action B27 are:

1. to investigate the modifications of HR variability during sleep in relation to different sleep stages;
2. to investigate (by means of statistical and nonlinear dynamic methods) the influence of the central nervous system to the control of HR in different states by means of HR variability analysis during sleep;
3. to investigate chaotic behavior of HR in different states of organism and its relation to regulatory mechanisms;
4. to investigate possibilities of identification of sleep stages using HR records during sleep.

The regulatory mechanisms will be investigated in different states (wake, somnolence, sleep) depending on state of central nervous system and psychological state of individual. HR variability will be investigated by means of nonlinear methods (empirical mode decomposition, Liapunov exponents, detrended fluctuation analysis etc.), and the results will be compared with the results obtained by the traditional methods (e.g., spectral, wavelets) with respect to identifiability of sleep states.

The web based data bank (http://www.pri.kmu.lt/datbank/) including records of HR during sleep is created. The data will be used to develop, identify and validate mathematical models of regulation of psycho-physiological processes. The time series of RR intervals collected in the data bank will be processed by traditional and nonlinear methods. The peculiarity of HR control during different sleep stages under various states of central nervous system will be considered, and the informative parameters for model creation will be selected. The project includes creation of theoretical model of relation between the states of the central nervous system and the HR variability, methods of visualization of the data and results, and methodology to assess adequacy of the model. The developed theoretical models will be helpful to create new methods for diagnostics of sleep states.

In 2006, application of methods of singular spectrum analysis and empirical mode decomposition for the identification of sleep stages as well as comparison of the results with those obtained with the conventional methods will be done.

COST Action B27

ELECTRIC NEURONAL OSCILLATIONS AND COGNITION (ENOC)

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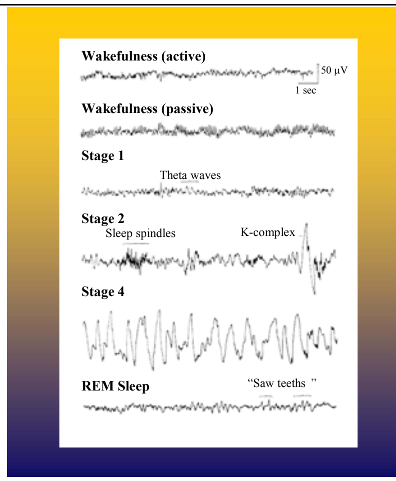
Theme: **Heart rate variability as a reflection of brain functions during sleep**

Research aims:

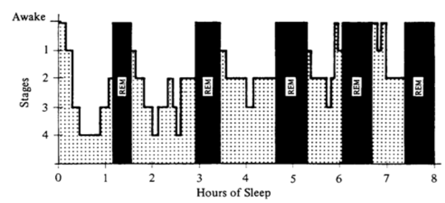
- to investigate the modifications of heart rate variability during sleep in relation to different sleep stages
- to investigate (by means of statistical and nonlinear dynamic methods) the influence of the central nervous system to the control of heart rate in different states by means of heart rate variability analysis during sleep
- to investigate chaotic behavior of heart rate variability in different states of organism and its relation to regulatory mechanisms
- to investigate possibilities of identification of sleep stages using heart rate records during sleep

Sleep Electroencephalography



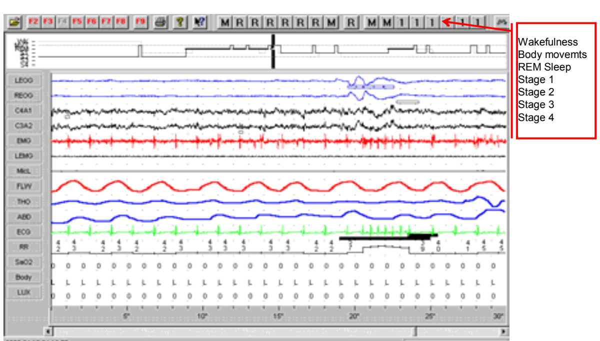
Normal Sleep Histogram

Sequences of States and Stages of Sleep on a Typical Night

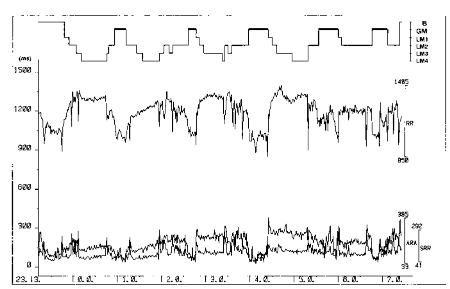


Identification and Staging of Adult Human Sleep. L.Shigley. Sleep Academic Award

Polysomnography



Heart Rate and Heart Rate Variability during Sleep

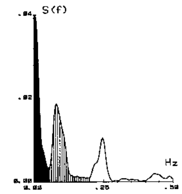


Zemaityte D. et al. Psychophysiology, 1984, 21(3), 279-289

Methods of obtaining the HRV parameters may by divided into following groups:

Time domain methods
Spectral domain methods
Non-linear methods
Mathematic modeling methods

HR analysis using power spectrum

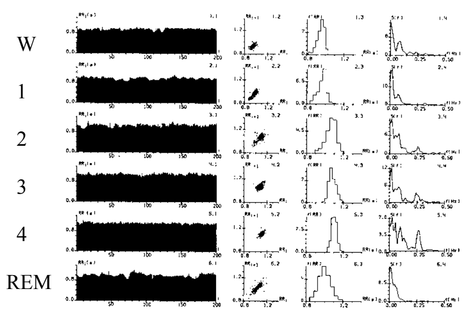


Three main oscillatory components:

very low frequency component (VLFC)
low frequency component (LFC)
high frequency component (HFC)

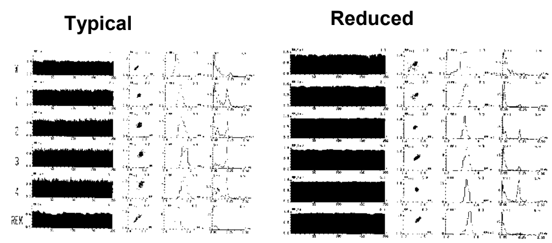
in absolute (ms) and relative (percent) values for evaluation:
humoral,
sympathetic-parasympathetic and
parasympathetic control, correspondingly

Heart Rate Sleep Pattern in Healthy Subject



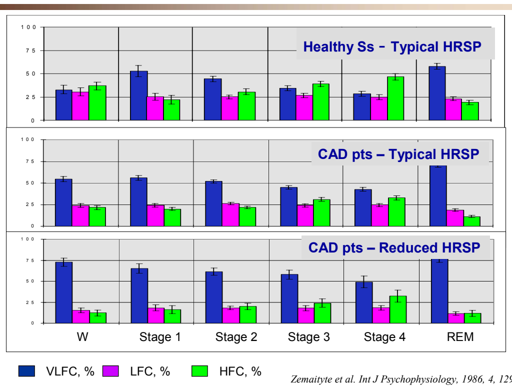
Zemaityte D. et al. Psychophysiology, 1984, 21(3), 279-289

Heart Rate Sleep Patterns during Sleep



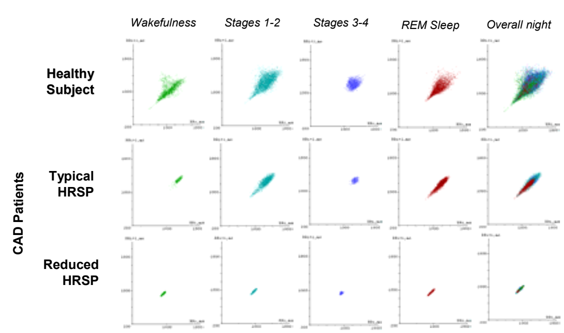
Zemaityte D. et al. Psychophysiology, 1984, 21(3), 279-289
Zemaityte D. et al. Psychophysiology, 1984, 21(3), 290-298

HR power spectrum components during different sleep stages



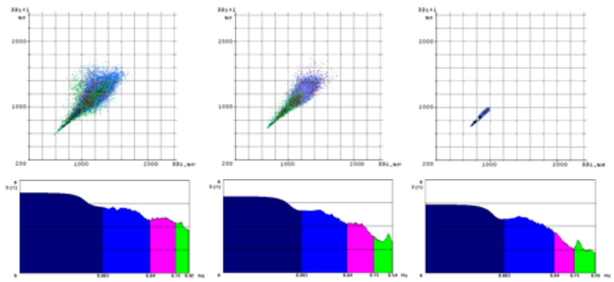
Zemaityte et al. Int J Psychophysiology, 1986, 4, 129-141

Poincare plots of RR intervals during individual sleep stages



Zemaityte D. et al. Biomedicine, 2001, 1, 1, 34-44

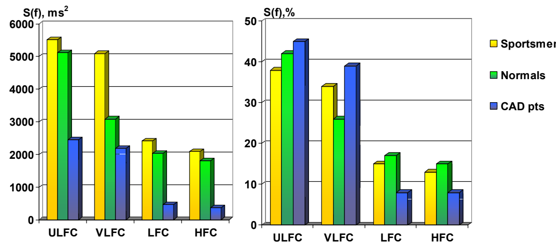
Poincare plots and power spectra of all-night HR recording



Sportsman | Healthy subject | CAD patient

Kesaite R..et al. Information Technology and Control, 2001, 2, 20-28

Absolute(ms²) & relative characteristics(%) of power spectra of all-night HR recording



Kesaite R..et al. Information Technology and Control, 2001, 2, 20-28

Correlation between individual parameters of Poincare plot and parameters of heart rate power spectrum (n=234)

	RR; ms	σRR; ms	ΔRR; ms	ULFC; ms	σVLFC; ms	σLFC; ms	σHFC; ms	ULFC; %	VLFC; %	LFC; %	HFC; %
RR; ms	0.99*	0.59*	0.55*	0.34*	0.57*	0.28*	0.43*	-0.32*	0.06	-0.02	0.28*
RR_{min}; ms	0.66*	0.03	-0.03	-0.15	0.03	-0.19*	-0.05	-0.10	0.10	-0.26*	0.21
RR_{max}; ms	0.82*	0.82*	0.77*	0.59*	0.71*	0.66*	0.68*	-0.47*	-0.21*	0.36*	0.39*
ΔRR_r; ms	0.55*	0.85*	0.83*	0.69*	0.75*	0.79*	0.68*	-0.46*	-0.24*	0.51*	0.28*
ΔRR_t; ms	0.37*	0.81*	0.74*	0.63*	0.62*	0.88*	0.84*	-0.48*	-0.49*	0.58*	0.48*
P; ms²	0.44*	0.85*	0.78*	0.66*	0.66*	0.89*	0.83*	-0.47*	-0.44	0.56*	0.44*

Zemaityte D. et al. Biomedicine, 2001, 1, 1, 34-44

Methods

Nonlinear analysis of continuous ECG during sleep: II. Dynamical measures *Fell J. et al. Biol. Cybern. 82, 485-91 (2000)*

The correlation dimension serves as an estimator of the number of degrees of freedom in a system, this is, the number of variables required to generate the observed dynamics

D2 - as a measure of the complexity of a time series *(Grassberger & Proccacia 1983)*

ECG dynamics was considered to be composed of two aspects: (i) the inter-beat or RR variability; (ii) the PQRST complex

- An increase in dominant chaoticity during REM sleep with regard to time-continuous nonlinear analysis is comparable to an increased heart rate variability
- The reduction in the correlation dimension (D2) may be interpreted as an expression of the withdrawal of respiratory influences during REM sleep

Tab. Contrasts between sleep stages for the nonlinear ECG measures D2, L1, K2 and average first return time (p = 0.05)

	D2	L1	K2	First return time
I II	n.s.	n.s.	n.s.	n.s.
I-SWS	n.s.	n.s.	0.022	n.s.
I-REM	0.011	n.s.	0.011	0.026
II-SWS	n.s.	n.s.	n.s.	n.s.
II-REM	n.s.	n.s.	n.s.	n.s.
SWS-REM	0.0022	0.0006	n.s.	0.013

Methods ***Detrended fluctuation analysis***

is able to separate the influence of sleep stages and sleep apnea on HRV

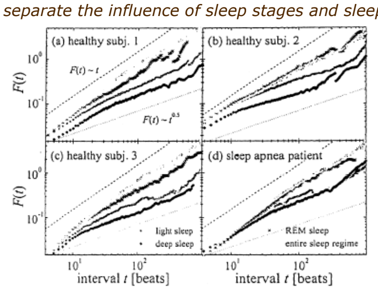


Figure 3: The results of the Detrended Fluctuation Analysis were plotted as the fluctuation function $F(t)$ over the intervals t for three healthy subjects (a-c) and one sleep apnea patient (d). The exponent α is the slope in the log-log plots. For 50 < t < 300, α is close to 0.85 for REM sleep (crosses) indicating long-range correlations, while α is close to 0.5 for light and deep sleep (filled symbols) indicating the loss of correlations.

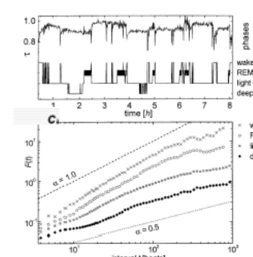
Penzel T. et al. Stud Health Technol Inform. 2000; 7:1256-60

Methods: ***Detrended fluctuation analysis***

Comparison of detrended fluctuation analysis and spectral analysis for HRV in sleep and sleep apnea: 14 healthy subjects, 33 pts with moderate, and 31 pts with severe sleep apnea

VLF, LF, HF, and LF/HF confirmed increasing parasympathetic activity from wakefulness and REM over light sleep to deep sleep, which is reduced in patients with sleep apnea

Analysis	Assignments for	
	apnea severity	sleep stage
Spectral	69.7%	54.6%
Discriminance	74.4%	85.0%



Changes in HRV are better quantified by scaling analysis than by spectral analysis

Penzel T. et al. IEEE Trans Biomed Eng. 2003;50(10):1143-51.

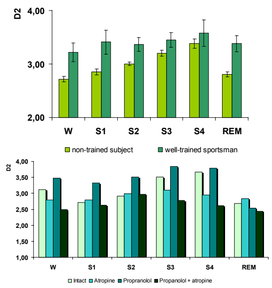
Non-linear Methods: *Correlation dimension (D2)*

The correlation dimension serves as an estimator of the number of degrees of freedom in a system, this is, the number of variables required to generate the observed dynamics

D2 - as a measure of the complexity of a time series *(Grassberger & Proccacia 1983)*

Non-linear Methods: *Correlation dimension (D2)*

Application of chaos theory in analyzing the HR in healthy subjects during sleep stages



$$d = \lim_{r \to 0} \frac{\log C}{\log r}.$$

$$C = \frac{1}{N_{p}} \sum_{i=1}^{K} \sum_{j=i+1}^{K} H(r - |X_i - X_j|).$$

The correlation between the changes in D2 during different sleep stages and the level of autonomic HR control was demonstrated

The chaotic element of HR, expressed numerically by D2 depends on the baseline level autonomic HR control

Eidukaitis et al. Human Physiology, 2004, 30, 5, 551-5

Background and Working Hypothesis

Heart rate and heart rate variability modifications during sleep reflect different autonomic control states influenced by central nervous system

HR and HRV oscillations during sleep might be used for identification of different organism states, i.e. sleep stages by Rechtschaffen and Kales (1968) or newly discovered

Sleep Heart Rate and Stroke Volume DataBank

http://www.pri.kmu.lt/datbank/

Multidimensional scaling for visualization of sleep stages using heart rate data

Multidimensional scaling is a method of the exploratory data analysis aiming to discover the structure of sets of objects using information on similarities/dissimilarities between those objects. $X_i \in R^n,\ i = 1,..,k$ $\quad Y_i \in R^2,\ i = 1,..,k$

interpoint distances $d_{ij}(Y)$ approximate interpoint distances $\delta_{ij} = \|X_i - X_j\|$

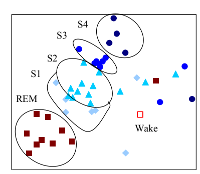
$$stress = \sum_{i=1}^{k} \sum_{j=i+1}^{k} w_{ij} \left(d_{ij}(Y) - \delta_{ij}\right)^2 \quad (1) \qquad sstress = \sum_{i=1}^{k} \sum_{j=i+1}^{k} w_{ij} \left(d_{ij}^2(Y) - \delta^2_{ij}\right)^2 \quad (2)$$

Visualization of sleep stages was performed using hybrid MDS of HR data during sleep. A MDS algorithm based on hybrid optimization of (1) and (2) combining evolutionary global search and local descent developed by the authors has been applied; for its details we refer to. In the subsequent sections, this algorithm is called *hybrid MDS stress* and *hybrid MDS sstress* indicating the optimization criterion: (1) or (2).

Podlipskyte et al. PRIP'2005: The 8nd International Conference on Pattern Recognition and Image Processing

Multidimensional scaling for visualization of sleep stages using heart rate data

Clusters of different sleep stages obtained from HR data using hybrid MDS algorithm



Distributions of HR sleep data on visualized pattern

Sleep stage	Inside the cluster	Outside the cluster
Stage I	66.7 %	33.3 %
Stage II	82.3 %	17.6 %
Stage III	71.4 %	28.6 %
Stage IV	80.0 %	20.0 %
REM sleep	81.8 %	18.2 %
Total (all stages)	79.2 %	20.8 %

Podlipskyte et al. PRIP'2005: The 8nd International Conference on Pattern Recognition and Image Processing

Multidimensional scaling for visualization of sleep stages using heart rate data

A hybrid MDS algorithm based on optimization of *stress* and *sstress* criteria, and combining evolutionary global search and local descent, can be used for visualization of sleep stages using HR data

This method allows to discriminate the clusters of points, representing individual sleep stages, in a two-dimensional plane

MDS can be also effectively used for establishing the informative HR pattern characteristics for classification of sleep states

Podlipskyte et al. PRIP'2005: The 8nd International Conference on Pattern Recognition and Image Processing

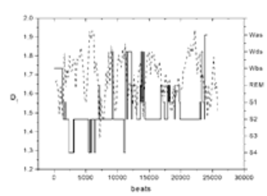
Non-linear analysis

- ❑The stochastic indexes of the regulatory systems functioning may be obtained by chaos analyses of the heart rate variability
- ❑Such indexes are thought to reflect the stress resistance of regulatory systems

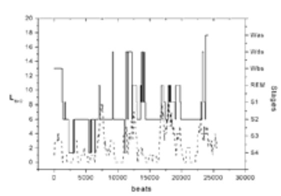
Klonowski et al. EMBEC05, 2005

Heart rate analysis during sleep

Higuchi's fractal dimension



Symbolic dynamics method



Klonowski et al. EMBEC05, 2005

Heart rate analysis during sleep

Plots of *Df* and *L4x0* values for time-course of night sleep demonstrate quasi-periodic oscillations, which correspond to the shifts of sleep stages during consecutive sleep cycles.

Changes of *Df* and *L4x0* values during night sleep can clearly reflect the transition from one to another state.

The obtained results confirm the nonlinear structure evidence in HRV data.

Methods

MATLAB package for analysis of RR sequences has been created including subroutines for estimation of linear and nonlinear functionals, e.g. spectral characteristics, approximated entropy, scaling exponent of detrended fluctuation analysis etc.

Parameters

- Mean
- Standard deviation
- Very low frequency component (VLF)
- Low frequency component (LF)
- High frequency component (HF)
- LF/HF
- Approximate entropy
- Scaling exponent (detr. fluct. anal.)
- Slope (progressive detr. fluct. anal.)

Questions

- ❑Are all the parameters important?
- ❑Are the parameters independent?

The goal of pilot study was to establish relations between the states of central nervous system (corresponding to REM and the first sleep stage) and heart rate variability

Informativeness of the estimated parameters with respect to characterization of REM and first sleep stages has been evaluated using multidimensional scaling based visualization

REM Sleep (red points) and Sleep Stage 1 (blue points)

Several popular classifiers have been compared: linear (LIN1, LIN2) and quadratic (QUAD) discriminant functions, minimal Euclidean and Malahanobis distance (EDIS, MDIS), support vector machine (SVM), artificial neural network (AAN)

Classifer	Dimensionality	
	9	5
LIN1	11.9	14.4
QUAD	13.6	14.6
MDIS	12.5	15.7
LIN2	11.7	12.2
EDIS	19.7	24.5
SVM	7.4	12.0
ANN	8.8	10.6

Errors of dichotomy of the training set (%)

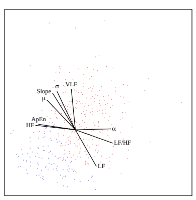


Image of the set of 9 dimensional points

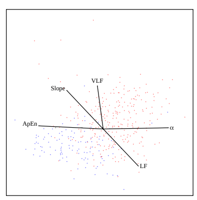


Image of the set of 5 dimensional points

Informative parameters

- Very low frequency
- Low frequency
- Approximate entropy
- Scaling exponent
- Slope

The indicated parameter set enables dichotomy between REM sleep and First stage sleep by means of simple linear classifier with accuracy approximately equal to 15%.

Choice of a classifier

Several popular classifiers have been compared: linear (LIN1, LIN2) and quadratic (QUAD) discriminant functions, minimal Euclidean and Malahanobis distance (EDIS, MDIS), support vector machine (SVM), artificial neural network (AAN).

Errors of dichotomy of the training set (%).

Classifier	Dimensionality	
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EDIS	19.7	24.5
SVM	7.4	12.0
ANN	8.8	10.6

Errors of dichotomy estimated 'jackknife' method (%).

Classifer	Dimensionality	
	9	5
LIN1	12.2	15.7
SVM	19.7	22.9
ANN	19.9	17.2

Linear discriminant function is the best

- ❑Minimal distance classifiers are least reliable
- ❑SVM and ANN are prone to overtraining

Theme: **Heart rate variability as a reflection of brain functions during sleep**

Research aims:

- to investigate the modifications of heart rate variability during sleep in relation to different sleep stages
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- to investigate chaotic behavior of heart rate variability in different states of organism and its relation to regulatory mechanisms
- to investigate possibilities of identification of sleep stages using heart rate records during sleep

Future plans for 2006

- ❑Application of methods of singular spectrum analysis and empirical mode decomposition for the identification of sleep stages
- ❑and comparison of the results with those obtained with the conventional methods

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ELECTRIC NEURONAL OSCILLATIONS AND COGNITION (ENOC)

Papers in 2005

❑***Zilinskas A., Zilinskas J., Varoneckas A.*** Computer aided system of heart rate data oriented to development of automatic diagnostics of sleep // Proceedings of International Conference CompSysTech, ISBN 954-9641-42-2, 2005, II.3-1-II.3.6.

❑***Zilinskas A., Zilinskas J., Varoneckas A.*** Linear and nonlinear methods in analysis of sleep stages with respect to heart rate // Proceedings of 8th International Conference PRIP 05, ISBN 985-6329-55-8, 2005, 26-29.

❑***Podlipskyte A., Varoneckas G., Zilinskas A.*** Visualization of sleep stages using multidimensional scaling of heart rate data during sleep // Proceedings of 8th International Conference PRIP 05, ISBN 985-6329-55-8, 2005, 34-37.

❑Klonowski Wl., Olejarczyk E., Stepien R., ***Varoneckas G., Alonderis A., Zemaityte D.*** Анализ вариабельности сердечного ритма во время сна методами фрактального и символьного анализа // Медленные колебательные процессы в организме человека. Теоретические и прикладные аспекты нелинейной динамики в физиологии и медицине. 2005. Новокузнецк, с. 57-62.

❑Klonowski W., Olejarczyk E., Stepien R., ***Varoneckas G., Alonderis A., Zemaityte D.*** Fractal and symbolic analysis of heart rate variability and sleep // The 3 European Medical and Biological Engineering Conference EMBEC05, November 20-25, 2005 Prague, Czech Republic. IFMBE Proceedings. ISSN: 1727-

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ELECTRIC NEURONAL OSCILLATIONS AND COGNITION (ENOC)

Papers in 2005

❑ ***Varoneckas G., Martinkenas A., Podlipskytė A., Varoneckas A., Zilinskas A.*** A web-based data bank of heart rate and stroke volume recordings during sleep // Proceedings of Med-e-Tel 2006: The International Trade Event and Conference for eHealth, Telemedicine and Health ICT: Luxembourg, April 5-7, 2006. ISSN 1818-9334. 2006. p. 371-375.

❑Penzel T., Canisius S., Becker H.F., ***Varoneckas G.***, Fietze I. Sleep analysis using new computer based methods In: T. Penzel, I. Fietze, S. Chokroverty (eds.) Proceedings of the World Association of Sleep Medicine 1st Congress. Medimond International Publ. Bologna, 2006, pp. 41-49.

❑***Eidukaitis A., Varoneckas G., Zemaityte D.*** Изменение нелинейных характеристик вариабельности сердечного ритма под влиянием физической нагрузки на функцию сердечно-сосудистой системы здоровых испытуемых и больных ИБС // Fiziologyja Celoveka. 2006, N 3. In press.

❑***Varoneckas G.*** Advanced sensoring of human physiological states using heart rate variability // International Journal of Applied Electromagnetics and Mechanics, 2006. In press.

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ELECTRIC NEURONAL OSCILLATIC
AND COGNITION (ENOC)

Presentati

- 8th International Conference on Pattern Recognition and Information Processing: Minsk, May 18-20, 2005.
- International Conference on Computer Systems and Technologies: Varna, June 16-17, 2005.
- The 4th Russian Symposium with international participation "Slow Oscillation Processes in Human Organism: Theory and Practical Application" and the 2nd Interdisciplinary School-Seminar "Nonlinear Dynamics in Physiology and Medicine", 2005, Novokuznetsk
- The 3 European Medical and Biological Engineering Conference EMBEC05, November 20-25, 2005 Prague, Czech Republic

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Presentati

- Med-e-Tel 2006: The International Trade Event and Conference for eHealth, Telemedicine and Health ICT: Luxembourg, April 5-7, 2006
- International Symposium on Sleep and Cardiovascular System, 6-8 April, 2006, Marburg, Germany
- Conference and meeting of the European Study Group on Cardiovascular Oscillations, 2006 May 15-17, Jena, Germany

Thank you for your attention