STATE OF THE ART AND NEW FRONTIERS IN SLEEP RESEARCH: NEW QUALITATIVE AND QUANTITATIVE APPROACHES

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Short summary: The electroencephalogram (EEG), electrooculogram (EOG) and electromyogram (EMG) are the basic measurements performed in all sleep laboratories (EEG + EOG + EMG = PSG or polysomnography). The Electrophysiological Profile of Sleep (EPS) is derived from PSG and contained 130 variables of nocturnal sleep. The results of our investigations demonstrate that the INDEX OF ENDOGENOSUS SLEEP PERTURBATION (IEP-P1 = REM - 1 / NREM - 1) is a highly reliable indicator of the development/regression of endogenic perturbation of sleep in depression, mania, schizophrenia, delusional state, organic brain syndromes and other altered states of consciousness. The sleep process is very important in many ways, but we point out the protection the brain of critical cooling and overheating. The sleep secure the brain (neurons) from crash because thermal excess.

The possible electromagnetic nature of sleep and of interneuronal (and extraneuronal) communications is the biggest challenge for further research of brain function.

Key words: Sleep, Sleep physiology, Sleep Disorders

A. EEG AND A SLEEP DISORDERS

1. THE SLEEP PROCESS

Sleep is regular, recurrent, easily reversible state of the organ-ism that is characterized by relative quiescence and by a great increase in the threshold of response to external stimuli relative to the waking state.(1)

The most important question in sleep research is: Why sleep ? What are the function of sleep ? Some researchers have even implied that sleep is a "vermiform appendix" that my have once served the function of keeping ancestors out of harm's way for a portion of the day but has no remaining function now. Most researchers believe that the sleep is – adaptive behavior (adaptation on day/night, light/darkness natural rhythm; or bioenergetic/thermoener-getic process who save the energy; or that sleep does serve some restorative function...

In our point of view, we hypothesized two most important functions of sleep; 1. the physiological function of sleep as a adaptive behavior is "saving the brain from critical cooling", and 2. the psychological function of sleep is "keeping the continuity of mental functions/psychic life through the "dream process". (Ilankovic N,1989)(10).

1.1 THE NEUROPHYSIOLOGY OF SLEEP

The waking state depends on the activity of the ascending reticular activating system (ARAS), which sends impulses to the forebrain for maintenance and physiological fluctuation of

cortical activity ("cortical tonus") as a basis for all cognitive functions. For some time after discovery of the ARAS (Moruzzi & Magoun,1949) it was assumed that sleep supervenes whenever ARAS activity falls below a certain level ("the passive theory of sleep"). The synchronized, "slow sleep" (NREM sleep) in animals is probably depends on the activity of certain "centers" in brain stem – especially the raphe nuclei (Moruzzi 1962, Jouvet, 1962, 1966) and certain areas in the medial forebrain ("the active theory of sleep"); other areas in the hypothalamus and the thalamus cannot be excluded. On the other side, a brain stem system is necessary for the initiating and maintenance of paradoxical "fast sleep" - REM (Rapid Eye Movement Sleep). A region in the lower brain stem containing giant cells - the frontal gigantocellular field (FTG) may play a direct role in initiating of REM sleep. McCarley and Hobson (1975) proposed that the states of sleep are regulated by a process of reciprocal inhibition between those FTG cells and the locus coeruleus. It seems likely that a reciprocal relationship involves the raphe nuclei and other areas in the addition to the relation between the FTG cells and the locus coeruleus... (Hartmann,1980).

Within that broad area, specific monoamine-containing pathways seem to be implicated in arousal or waking. The serotonin – containing raphe system is definitely necessary for normal sleep of both kinds (NREM, REM) to occur. The ascending noradrenergic system originating from the locus coeruleus and other brain stem norepineph – rine regions play an inhibitory role in REM sleep (Hartmann,1973).(1)

1.2 NEW FRONTIERS IN SLEEP RESEARCH

We are inclined in our new approach in explanation of sleep mechanism, to support hypothesis that sleep patterns and circadian cycle wakefulness-sleep, are building block in some greater natural rhythms, shaped by interaction of external stimuli and internal performances of CNS, with certain adaptive and protective feature.

Having that in mind, we have created the new, original hypothesis about PASSIVE AND ACTIVE PROTECTIVE "HELP" SYSTEMS, which, through sleep, protected the brain from critical COOLING and/or OVERHEATING. (Ilankovic N&A 1986,1990) (10)

1.2.1 THE SLEEP PROTECT THE BRAIN FROM CRITICAL COOLING AND OVERHEATING

In fact, reducing brain tissue's temperature would lead to regression of brain's electrical activity during NREM sleep, while through active processes of REM sleep metabolic homeostasis and homeothermic conditions would be regained. NREM periods are time when nature is trying to cut down some energy spending by "passively preserving it" – "PASSIVE HELP SYSTEM". This is managed by progressive inhibition of telencephalic activity and by marked reduction in muscle tone (disconnection of telencephalic region from rhombencephalic motor mechanisms). Since inactivation of great muscle groups is offering bad "saving plan" due to their significant role in thermoproduction, "ACTIVE HELP SYSTEM" is handling this thermonergetic disbalance and keeping the brain away from critical cooling point – through REM sleep active neuronal and metabolic processes in brain stem are released. They include increased cerebral blood flow, increased glucose utilization and rising brain tissue's temperature! Thanks to these active processes, brain is protected from critical cooling and yet another life saving and function preserving mechanisms are in effect. The role of cerebrospinal fluid and the circulatory and respiration systems is very important in this thermoregulatory processes, too. (Ilankovic A., 2000).

Our hypothesis tackles not only well known electro–chemical processes in neuronal functions, but also some phenomena concerning ELECTRO–MAGNETIC INDUCTION in interneuronal communications (Ilankovic N,1990, 2000). We assume that the very fast "switch" in thermoregulation of/in brain, is electromagnetic phenomena, too. (Ilankovic N&A, 2001) Investigations of these phenomena should be in focus of research in new "Sleep Center" of University Clinical Center in Belgrade.

1.2 SLEEP AND DREAM

Many psychological and psychophysiological studies indicates that the both electrophysio–logical type of sleep are identifiable different in mental activity.

The mental activity in NREM sleep is generally less vivid, less visual, less well recalled, more conceptual, more plausible, less bizarre, more like thinking than dreaming , less emotional, more concerned with contemporary waking experience and under greater volitional control.

On the other side, the mental activity in REM sleep – dreaming, have the opposite characteristic. The dreams have other language, different symbolism with individual and collective meaning, altered dimensions of time and space (similar to the altered state of consciousness).

Freud's observation that state of sleep makes the formation of dreams possible by a reduction of the power of the censorship ("the way to unconscious..."), may have a neurophysio-logical analogy in the activation of REM through the activation of rhombence-phalic and associated limbic circuits in relation to the reduction of controlling influences flowing from the corticofugal inhibitory systems...

Freud also viewed the dream process as a regressive mental functioning in the sleep state (1933.). The regressive form of mental functioning in the dream process can be connected to the rhombencephalic pattern of sleep that is both ontogenetically and phylogenetically the more primitive form of sleep activity - Jouvet (1966) referred to such REM activation is "archisleep".

Modern neurophysiological research has opened up new vistas in the understanding of the mechanisms of the dreaming process. Two basic and conflicting hypotheses remain: 1. Freud's basically psychological hypothesis of diminished endopsychic censorship; and 2. Psychophysiological hypothesis of spontaneous activation of neuronal circuits as the underlying cause of dreaming activity. In our hypothesis (Ilankovic,1986) the REM sleep (as a one dimension of very complex dreaming process) has the underlying mechanisms in electromagnetic phenomena through the sleep.(10)

The explanations of functions of dreaming activity are hypothetically, too. Some scientist said: all is in Freud's works; other (psychophysiologist) - in "dream activity" the important process is the work up of visual informations, selection and memorizing some of them. The hypothesis about "cleaning" function and tendency to "equipotentiallity" of information through dreaming, is the very current theory today.(2)

1.3 NEW HYPOTHESIS ABOUT FUNCTIONS OF NONREM AND REM SLEEP

THE ROLLES OF REM SLEEP IN "INTRANET–COMMUNICATION":
In REM–sleep ("dreams") the brain works on:
selection and saving of informations,
· "compression/decompression" ("pack/unpack") the memory data,
· creating the new "short-cuts" (symbols),
· "clean-up" of memory data/informations,
· on "upgrading" the programs with new informations / experiences / learning (with data from "intranet-communication" and training of neuronal networks; and from external "internet-communication", too ?)

THE ROLLE OF NONREM SLEEP IN "INTERNET–COMMUNICATION":
1. The reduction of vigilance in NonREM–sleep is a conditio sine qua non for "CONNECTION" and "LOGGING ON THE NETWORK",
2. NREM–SLEEP is a basis/introduction for "COMMUNICATION–SLEEP" or REM-SLEEP (N.Ilanković,1999.),
3. REM-SLEEP is a state / time of "SURFING" on the network, "DOWNLOADING" and "UPGRADING" of "programs" and "data basis"?

SLEEP/DREAMS AS A HYPOTHETIC COMMUNICATION STATE
"As a further determinant of dreams I have acknowledge the TELEPATHIC phenomenon. Today we can not doubt in reality of that phenomenon... It is very easy without checking of the existing proof material to deny existence of this phenom-

enon – but that would be unscientific behavior, which doesn't deserve our attention! (Jung).

2. THE SLEEP DISORDERS

Sleep disorders are major psychiatric disorders that affect up to 30 percent of the population. In many sleep disorders a careful diagnostic workup reveals a specific cause of the insomnia and a specific treatment aimed at the cause may be used.

There are two major categories of sleep disorders in the revised third edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R) (3):

1.The DISSOMNIAS and
2.The PARASOMNIAS.

The DISSOMNIAS are:
a) Insomnia (difficulty in falling asleep),
b) Hypersomnia (excessive amounts of sleep or complaints about excessive daytime somnolence), and
c) Sleep-Wake schedule disorder.

The PARASOMNIAS are a heterogeneous group of disorder in which episodic nocturnal events occur during sleep or at threshold between wakefulness and sleep.

Very similar is the diagnostic classification of the Association of Sleep Disorders Centers (ASDC) with about 80 sleep disorders in 4 diagnostic groups (4):
1. Disorders of Initiating and Maintaining Sleep (DIMS),
2. Disorders of Excessive Somnolence (DOES),
3. Disorders of the Sleep-Wake Schedule, and
4. Parasomnias.

3. ELECTROENCEPHALOGRAPHY (EEG) OF HUMAN SLEEP - A HISTORY

Scientific sleep research began little more than 120 years ago and may be divided into two eras:
1. Pre-EEG era, the period from about 1860 to 1935,
2. EEG era, the period from 1935 to the present.

3.1 PRE–EEG ERA

Prior to the development of EEG researchers employed a variety of measures to describe human sleep. These included threshold determinations, physiological measures such as body temperature, heart rate, respiration, pupillary size, metabolic rate, galvanic skin response (GSR) and electromyogram (EMG). In addition, monitoring of body movement was an extensively used technique.

Wohlish (1957) documented the beginning of scientific inquiry into sleep in his account of the thresholds experiments of Kohlschuter in 1860. Wohlish also described Fechner's account of what may be the first attempts to measure sleep "whereby the strength of sound necessary to awaken a sleeping person can be used for the measurement of the depths of sleep" (Fechner, 1860). Over the years many attempts have been made to measure and describe the depth of sleep in relationship to the strength and subjective relevance of various stimuli required to produce arousal.

Body movement during sleep was also extensively measured prior to the period of EEG, but one of the most commonly used indices was a sleep duration. In the midst of these widespread efforts to peer into to dark world of the sleeping subject came the interesting but seemingly irrelevant news in 1875 that Caton had detected currents from electrodes placed on the skull or the exposed brains of rabbits and monkeys.

However, it is cause for some wonder that no one was interested in the work of HANS BERGER some fifty years later, when in 1924 he recorded the first human EEG from electrodes on the scalp. Sleep researchers of the day paid no attention whatsoever, and when Berger undaunted, published his work in 1929, the scientific community in general greeted the news with incredulity. It is interesting to note that Berger was not the only one whose EEG findings were not accepted. A medical student at Harvard Donald Mc Pherson in 1918, noted regular 10 per second waves recorded from electrodes placed on an exposed cat brain. However, when his superior criticized his findings as artifact, he pursued the dis-

covery no further and the tracing was not found until 1944 when the laboratory was being cleaned of old materials! Gibbs and Gibbs (1951) suggest that Berger's work unheralded because he was a psychiatrist and published his work in psychiatric journals under titles that were "not especially informative", and that if Berger had "divided his work into discrete short studies, with satisfactory descriptive titles, and had avoided the psychiatric implications of his data, he might have been accepted more readily as a great neurophysiologist..." Herbert Jasper (1969) comments:"...It seemed highly unlikely at that time that the simple rhythmic waves, the "Alpha und Beta Wellen" of Hans Berger could possibly represent the true electrical activity of such complex nerve tissue as the cerebral cortex especially in man, recorded not by experienced electrophysiologists but by a PSYCHIATRIST with rather crude and simple apparatus..." Whatever the reason, Berger's work did not receive recognition until prominent fellow investigators such as Lord Adrian (1934) began to confirm his studies.(5)

3.2. THE EEG–ERA

The history of human EEG essentially begins with the acceptance of the work of Hans Berger. Sleep research, developing along other lines, did not immediately take advantage of this technique.

The EEG era in sleep research may be said to have begun in 1935 when LOOMIS, Harvey and Hobart, made the first classification of the electrical activity of the human brain during sleep. These investigators described five different patterns of electroencephalographic activity which they labeled A through E, and which they reported could be observed with different states of or levels of sleep. They suggested that a change in level of consciousness was connected with each change in wave-type. However, it was not until 1953 when ASERINSKY and KLEITMAN first reported that sleeping subjects typically exhibited two kinds of eye movements, slow and rapid, that the scientific world was really awakened to the implications of the Loomis et al. work. In expanded study reported in 1955, Aserinsky and Kleitman investigated the rapid eye movement (REM) sleep state and its relation to dream reports and found that the slow eye movements occurred in three-to-four second intervals and the REM appeared in clusters that recurred several times during the night. When subjects were awakened during the REM periods, 20 out of 27 replies detailed dream descriptions; in contrast 19 out of 23 subjects awakened during Non-REM (NREM) periods reported no recall of dreaming.

The importance of Aserinsky and Kleitman's discovery was emphasized by DEMENT's classic demonstration of the "need" for REM sleep (1960). Dement found that after repeated awakenings from REM sleep, on subsequent night of undisturbed sleep a higher average amount of REM was observed (REM-compensation). The discovery of the REM state sparked renewed interest in the examination of physiological measures during sleep. It has now been shown that REM periods are accompanied by: a general increase in autonomic activity including heart and respiration rates and systolic blood pressure; a greater frequency of nocturnal penile erections; an increase in level of oxygen consumption; a decrease in oxygen supply; an increases in the secretion and osmolality of urine and changes in the circulating levels of plasma 17-hydrocorti-coids; a general desynchronization of neural firing and an increase in neural activity in the motor and sensory areas of the brain; an increase in cerebral blood flow; a rise in brain temperature; and a decrease of tonic muscle activity (muscle tone in head and neck, reduction in spinal H-reflex).

WILLIAMS, AGNEW and WEBB began at the University of Florida Sleep Laboratories in the early 1960s to establish baseline for EEG sleep in normal humans. The original objective in investigating normative sleep EEG patterns of all age groups was to describe the ontogenetic progression of human sleep pattern and to provide baseline data for later studies of sleep disorders and for studies of the relationship of sleep and sleep disturbances to psychopathology.

4. EEG AND A SLEEP DISORDERS

The discovery of the human electroencephalogram (EEG), followed by the technology to study the electrophysiology of sleep, has made

possible objective measurements of patients suffering from sleep disorders. The advent and development of computer technology has made the storage and the analysis of EEG sleep data quicker, less complicates and less expensive.

The electroencephalogram (EEG), electrooculogram (EOG) and electromyogram (EMG) are the basic measurements commonly performed in all sleep laboratories (EEG + EOG + EMG = PSG, POLYSOMNOGRAPHY). In addition, the electrocardiogram (ECG), blood pressure, respiration rate and amplitude, plus a variety of special measurements such as penile tumescence, penile blood pressure, blood oxygen saturation, temperature, and others.

The etiology of most sleep disorders is not known; however, PSG studies have made it possible to describe both qualitatively and quantitatively the electrophysiological characteristics of normal and disturbed sleep. Numerous sleep-variables have been examined and although may differ from laboratory to laboratory and from study to study, there are certain dimensions of sleep which are being examined in sleep disorders. Some of more frequently used include (6):

1. The TIME IN BED (TIB) which is measured from the time the subject is settled in bed until the EEG is turned of in the morning (mean by 20-29 old males - 442.23 min);
2. The SLEEP PERIOD TIME (SPT) which is the time in bed less the time it took the subject to fall asleep after the lights were out and less the time he lay in bed after awakening in the morning (mean - 424.64 min);
3. The TOTAL SLEEP TIME (TST) which is the sleep period time less any time the subject spent awake during the night after the initial sleep onset;
4. The PERCENTAGE OF EACH SLEEP STAGE (stage 1,2,3 and 4 NREM, and REM-period) which is usually computed as a percentage of the sleep period time that is occupied by a given sleep stage;
5. The SLEEP ONSET LATENCY which is considered to be the time from lights out until the appearance of the first or second sleep stage;
6. The NUMBER OF STAGE SHIFTS which is the number of times sleep changes from one stage to another;
7. The NUMBER OF AWAKENINGS (NAW) as indicated by the presence of "stage 0" are commonly counted;
8. The LATENCY OF EACH SLEEP STAGE which is the time from sleep onset to the appearance of a given stage;
9. The STAGE SEQUENCING which is the order of appearance of each sleep stage; it has been reported in the normal sleep profiles and in the study of some sleep disorders;
10. The SLEEP EFFICIENCY INDEX which is measure derived by dividing the total sleep time by time in bed;
11. The number of RAPID EYE MOVEMENT (REM) PERIODS, the REM PERIOD LENGTH, the REM INTERVAL an the REM DENSITY, all of which are measures which have been examined in normals and may be important in understanding certain sleep disorders.
12. The RATIO OF REM SLEEP TO NON-REM SLEEP (I.E.P, Index of Endogenous Perturbation; Ilankovic, 1983.) has been studied in normals and appears to be important in understanding sleep disorders. (7)

In our studies ("Sleep Center Belgrade") after analysis of polysomnogram (PSG), 130 basic and derived parameters were designated as the "ELECTROPHYSIOLOGICAL PROFILE OF SLEEP" (EPS) (8)

4.1 THE ADVANCE IN TECHNOLOGY OF POLYSOMNOGRAPHY

The classical registration and analysis of polysomnography (EEG + EOG + EMG) is made according to accepted standards (Rechtschaffen and Kales,1971)(7). In sleep laboratory it is a registration over the night (from 10 p.m. to 6 a.m.) or over 24 hours with many limitations.

The big advance in technology of polysomnography is the utility of AMBULATORY POLYSOMNOGRAPHY, which implies the recording of physiologic data during sleep from a subject who is free from attachment to stationary physiologic recording devices.

The earliest methods of ambulatory monitoring employed the transmission of data to a remote display and/or recording device. Data transmission was accomplished using radio fre-

quencies and telephone. These methods were employed as early as 1921. for EKG, and 1949. for the recording of EEG. However, the technologist must go to the home of the patient at the beginning and end of study to attach electrodes , set up equipment, establish the telephone connection and reverse the process of the end of the study.

More recently developed ambulatory monitoring systems allow for the recording of data on a tape recorder directly attached to the patient /subject - CASSETTE POLYSOMNOGRAPHY. These devices currently record in an analog mode and can store large amounts of data on an inexpensive medium (audiotape). Although the "Holter Electrocardiographic Monitor" was first designed in 1961, a multichannel recorder suitable for polysomnographic application did not become available until 1971. WILKINSON was the first to report polysomnographic cassette monitoring of acceptable technical quality in 1973.(9)

4.2 CLINICAL APPLICATIONS OF CA SETTE POLYSOMNOGRAPHY IN SLEEP AND SLEEP–RELATED DISORDERS

The ASDC (Association of Sleep Disorders Centers) nosology divides the sleep disorders into four large groups: 1. DIMS (insomnia), 2. DOES (excessive somnolence), 3. Disorders of sleep-wake schedule, and 4. The dysfunctions associated with sleép, sleep stages, or partial arousals (parasomnias).

1. INSOMNIA is a disorder of initiating or of maintaining sleep (DIMS). Ambulatory cassette polysomnography (ACPSG) in patients with insomnia has demonstrated sleep apnea, narcolepsy and periodic (leg) movements (PLM) in more than 70 % of cases. Many patients has elevated Number of Awakenings (NAW) - fragmentation of nocturnal sleep, according to our Model of Exogenous Sleep Perturbation (Ilankovic, 1983.)(7)

2. HYPERSOMNIA disorders are also known as disorder of excessive somnolence (DOES). The patients with hypersomnia have two group of symptoms: complaints about excessive amounts of sleep and complaints about excessive daytime sleepiness (somnolence). According to a recent survey, the most common conditions responsible for hypersomno–lence severe to enough to be evaluated by all–night recordings or by ambulatory cassette polysomnography (ACPSG), were sleep apnea and narcolepsy. ACPSG in patients with narcolepsy has demonstrated: multiple brief spontaneous naps, many with sleep–onset REM periods (SOREMPs), and disrupted nocturnal sleep. A day time Multiple Sleep Latency Test (MSLT) – several recorded naps at two–hour intervals shows very rapid sleep onset an usually one or more SOREMP. NREM–narcolepsy is a idiopathic or symptomatic (!) hypersomnolence and it is characterized by recurrent daytime sleepiness, but sleep attacks (cataplexy, sleep paralysis) do not occur, because the sleepiness is not as irresistible as in narcolepsy (REM-narcolepsy).

3. Extended monitoring (ACPSG) my be most directly applicable to DISORDERS OF THE SLEEP-WAKE SCHEDULE. These disorders are characterized by the patients inability to wake at desired times despite achieving normal overall amounts of unimpaired sleep or to sleep at the desired time despite a normal preceding period of wakefulness. These disorders are truly circadian in nature and demand extended monitoring for thorough evaluation. Among the more common of the disorders of sleep-wake schedule is that occurring with changing shift work. The implications for worker safety and productivity are enormous. "Jat lag syndrome" is the other most common type of this disorder. Long-term ambulatory temperature monitoring has been useful in understanding delayed sleep phase syndrome.

4. Reports concerning the use of ACPSG for PARASOMNIAS are yet forthcoming. The combination of ambulatory monitoring and videotape monitoring is helpful in diagnosis for certain parasomnias e.g. sleepwalking, sleep terror disorders (both - stage 3,4 NREM), nightmare (REM), head banging (pre-sleep period or light sleep), ect.

In addition to these applications, ACPSG has begun to uncover the relationship between sleep and various medical disorders. The peak time of day for sudden cardiac death occurs at the REM-sleep rich period of 5 to 6 a.m.

ACPSG has been employed to study the relationship of ventricular ectopia to sleep stages.

Ambulatory monitoring has been applied to other systemic dysfunctions associated with sleep, including esophageal reflux, impotence, ect.

B. A NEW QUANTITATIVE APPROACH

1. AIM OF OUR STUDY AND METHODOLOGY

In our study on the example of the depressive disorders, we would like to point out the importance of the measurable variables of Electro–physiological Profile of Sleep (EPS) as the components in differential diagnosis of reactive and endogenous mental diseases (EPS= 130 variables of nocturnal sleep derived from PSG = polysomnography = EEG + EOG + EMG).

The sleep disturbance very frequently seen in depressive conditions is the initial basis for the discovery of certain neurophysiological parameters of nocturnal sleep that could be used as indicators of endogenic perturbation in chronobiological functions of brain. (8)

Selection of the sample (90 patients with "maior–depression" according DSM–III–R 30 reactive + 30 endogenous depression; and 30 patients with acute schizophrenia), precise neurophysiological measuring (PSG) and exact statistical testing (MVA, Discriminative analysis "step by step") result in establishing new indicators of changes in internal sleep organization as factors used in the appraisal of the qualitative switch from the biologically adapted state to the devel–opment of biological/endogenic perturbation.

2. DISCRIMINATIVE PROFILE OF SLEEP (DPS)

In this way, using only 2 parameters of EPS (of 130 available) of the first period of nocturnal sleep (registration time is shortened from 8 to 1 hr !), the problem of exact classification of new patients in group with and without endogenic perturbation of sleep (with reactive and with endogenic depression), seems easier to solve.

Practical application can be seen in the following example of classification function – "Discriminative Profile of Sleep", DPS):

STAD-1,4 (4th stage of the 1st period)
REM-1 (first REM period, SOREMP)
(k1 - k2) x STAD-1,4 + (k1 - k2) x REM-1 =
> = K1 - K2 (exogenous depression)
< K1 - K2 (endogenous depression)
k1=1.023 k2=0.135 (for STAD-1,4)
k1=1.263 k2=1.935 (for REM-1)
K1=-44.565 K2=-66.789

3. THE MODELS OF EXOGENOUS AND ENDOGENOUS SLEEP PERTURBATION®

The statistical MODEL OF EXOGENOUS PERTURBATION OF SLEEP, characteristic of exogenous/reactive (depressive) states consists of:
1. The increased Number of Nocturnal Awakenings (NAW) – statistically the most important phenomenon
2. Shortened REM-sleep,
3. Prolonged first sleep period,
4. Decreased REM/NREM Ratio.

The indicators of development (progress /regression) of endogenic perturbation are also determined:
1. Decreased NAW,
2. Reduction of "delta-sleep' (stages 3 and 4 NREM),
3. Shortened first period of night,
4. Increase of total Wakefulness.

The statistical MODEL OF ENDOGENOUS PERTURBATION OF SLEEP found in endogenic depression (but in mania, OMD, schizophrenia, paranoid states, anorexia, alcoholism, and in different time of development/maturation of human brain, too !), is composed of the next parameters of nocturnal sleep in two opposite situations:

I MODEL - "DELTA DEFICITE TYPE" :
(with reduction of "delta-sleep")
– in endogenous depression and delusional states

(N. Ilankovic,1996) –
1. Shortened REM-latency,
2. REDUCTION OF "DELTA-SLEEP",
3. INCREASED of Index of Endogenic Perturbation (IEP),
4. Prolonged REM-l phase (SOREMP)

II MODEL - "REM DEFICITE TYPE":
(with reduction of REM-1 phase)
– in schizophrenia-like states (N.Ilankovic,1996) –
1. Prolonged REM-latency,
2. Disturbed "delta-sleep",
3. DECREASED of Index of Endogenic Perturbation (IEP)
4. Reduction of REM-1 PHASE (SOREMP)

4.INDEX OF ENDOGENOUS PERTURBATION OF SLEEP (IEP)®

Neurophysiological measurements of the internal organization of sleep (REM/NREM alteration) in our studies was exposed to special statistical testing – the parameter approach in discriminative analysis. (9)

The results of our investigations demonstrate that the parameter INDEX OF ENDOGENOUS PERTURBATION OF SLEEP (IEP, N.Ilankovic,1983,1986,1995) is a highly reliable indicator of the development /regression of ENDOGENIC PERTURBATION OF SLEEP in depression, mania, schizophrenia and other psychotic states (altered states of consciousness), organic brain syndrome, ect.

IEP-P1 = REM-1 / NREM-1 ...Index of Endogenous Perturbation

5. AGE, IEP-P1 AND THE SPECIFIC MENTAL STATES

In healthy child who is 30 weeks old IEP = 4 , in 1st year >1, in healthy adult (25 years old) the mean value of IEP = 0.44, in old men (60 - 70 years old) < 0.4.

In REACTIVE (depressive) states the IEP value is light elevated IEP-P1=0.77 .

In ENDOGENOUS (depressive) states and in other states of altered mental func-tion, altered states of consciousness and in specific psychotic states (schizophrenia–like and delusional states or hypothetically "transcomunnication states" according clinical phenomena, N. Ilankovic, 1986, 1995, 1996) (11) the alteration of sleep periodicity is very deep and the Index of Endogenous Perturbation (IEP-P1) is or very HIGH (I) or very LOW (II):

I MODEL – "DELTA DEFICITE TYPE" :
(with reduction of "delta-sleep")
–in endogenous DEPRESSED, MANIC, and PARANOID states:
"HYPER-COMMUNICATION states", (Ilankovic,1986.)

IEP-P1 > 2.40 !

II MODEL - "REM DEFICITE TYPE":
(with reduction of "REM-1 phase")
in SCHIZOPHRENIA-like states:
"HYPO- and A-COMMUNICATION states", (Ilankovic,1986)

IEP-P1<0.30 !

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6. CONCLUSION

1. The sleep process is very important in many ways, but we point out the protection the brain of critical cooling and overheating. The sleep secure the brain (neurons) from crash because thermal excess.
2. The importance of the INDEX OF ENDOGEMIC PERTURBATION OF SLEEP (IEP) can be seen in clinical approach (in classification of different states/type of mental illnesses, evaluation of therapy, course and prognosis).
3. The IEP can be useful in further research of chronobiological mechanisms of brain, too: chronobiological plasticity of brain, BIOLOGICAL AGING OF BRAIN, SPECIFIC STATES OF ALTERED CONSCIOUS–NESS and in biophysical modeling of brain mechanisms of sleep and neural functions.
4. The possible electromagnetic nature of sleep and of interneuronal (and extraneuronal) communications is the next biggest challenge for further research of brain function.

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DOSADAŠNJA ZNANJA I NOVI PRAVCI U ISTRAŽIVANJU SPAVANJA: NOVI KVALITATIVNI I KVANTITATIVNI PRISTUPI

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Abstrakt: U ovom revijalnom radu se prikazuju dosadašnja znanja o istrazivanjima fiziologije i patologije spavanja, rezultati sopstvenih kliničko-neurofizioloških istraživanja, putevi daljih istraživanja i nove hipoteze o funkcijama spavanja i sanjanja.

Proces spavanja ima višestruki fiziološki i psihološki značaj. Naša hipoteze ističu fiziološki, homeostatski značaj spavanja u zaštiti mozga od kritičnog rashlađenja i pregrevanja /zastita neurona od termickih ekscesa/, i funkciju spavanja i sanjanja u odrzavanju kontinuiteta svesti.

Rezultati naših istrazivanja su ukazali da je INDEKS ENDOGENE PERTURBACIJE SPAVANJA /IEP-P1=REM-1:NREM-1/ visoko validan indikator razvoja ili regresije endogene perturbacije spavanja kod endogene depresije i manije, akutne shizofrene psihoze, paranoidnih stanja, organskih mentalnih poremećaja i drugih izmenjenih stanja svesti.

Najveći izazov u daljim istraživanjima procesa spavanja su elektromagnetni fenomeni od značaja za intèrneuronalnu /i ekstraneuronalnu?/ komunikaciju u CNS, posebno u toku spavanja, sanjanja, prelaznih i izmenjenih stanja svesti.

Ključne reči: Spavanje, Fiziologija spavanja, Poremećaji spavanja