Chapter

Sleep Physiology and Polysomnogram, Physiopathology and Symptomatology in Sleep Medicine

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Abstract

Over recent years, the importance of sleep physiology and pathology has been better understood in terms of correct diagnosis, treatment, prognosis and innovative research of diseases. Sleep disorders are often confused with clinical symptoms of adult and pediatric medical conditions. In medicine, electrophysiological signal recording methods are very important for establishing a correct diagnosis especially in neurological sciences. Polysomnography (PSG) is a golden standard diagnostic method that records electrophysiological signals used for sleep physiology and diseases. When the medical disciplines and diseases that make use of this diagnostic method are considered, its significance becomes clearer. For example, medical disciplines benefiting from PSG are as follows: "Clinical Physiology, Neurology, Ear Nose and Throat, Dentistry, Psychiatry, Pulmonology, Cardiology, Pediatric Neurology, Pediatric Cardiology, Internal Medicine, Neurosurgery, Endocrinology, etc." The patient groups diagnosed with PSG are as follows: "Sleep Disordered Breathing (Central Sleep Apnea Syndrome, Obstructive Sleep Apnea Syndrome), Obesity, Morbid Obesity, REM Behavior Disorder, Restless Leg Syndrome, Rhythm Disorders, Epileptic Disorders, Insomnia, Insomnia and Headache, Hypersomnia, Narcolepsy, Secondary Hypertension, etc." Interpretation and understanding electrophysiological signals correctly show us interactions of body systems with sleep physiology and integrated therapeutic approaches to sleep disorders. In conclusion; new approaches to sleep pathophysiology depend on a better understanding and further advancement of polysomnography.

Keywords: electrophysiology, awake, sleep, mechanism, PSG, correct diagnosis, innovation

1. Introduction

Electrophysiological signal recordings are used in medicine for research, clinical diagnosis and follow-up of diseases as well as for providing guidance to their treatment. For example; "Electrocardiogram (ECG)" is used daily as inpatient

and as outpatient, it is the most basic electrophysiological signal recording in which five waves (P, Q, R, S, and T) are interpreted. When all monitorization activities performed at the bedside of the patient are taken into consideration, recording electrophysiological signals with well-calibrated equipment and correct interpretation of the obtained results by doctors and healthcare staff seems to be at the crossroads of correct diagnosis, follow-up and treatment. In sleep monitorization, electrophysiological signal recordings are performed by multiple electrodes and provide us with important clinical information. In fact, monitoring wakefulness as much as sleep is quite important in clinical practice; it helps to establish a correct diagnosis in clinical practice and sometimes provides the opportunity to have access to unsuspected information. If PSG could be used as frequently as ECG by well-trained medical doctors and healthcare personnel in sleep medicine, sleep health and sleep disorders of the individuals in the society could be understood much better. Therefore, health could be evaluated not only in wakefulness but also in sleep leading to a continuum. During its preliminary years, sleep related studies attracted the attention of physiologists and as time passed clinical information regarding sleep disorders increased significantly and the possibility to treat all these diseases brought the attention of clinicians into this field. For human physiology and especially for the central nervous system to continue its functioning; there needs to be a healthy interaction and an organism specific balance between wakefulness and sleep cycles. Sleep is a physiological need; a state where the response of the brain to environmental stimuli has stopped reversibly. The insufficiency or absence of this need negatively influences the interactions in the neuronal circuits and pathways that are responsible for the wakefulness of the brain. It is very well known that many functions of the organism change during sleep and different physiological mechanisms come into play during NREM and REM sleep. Diseases also show changes during sleep and during NREM and REM phases. Electrophysiological studies could assist in the understanding of basic mechanisms in neurological sciences. Electrophysiological methods and PSG that are geared to understand the nights as well as the days aim at not only establishing correct diagnosis and delineating pathophysiological mechanisms but also engaging in innovation and developing novel diagnostic and therapeutic methods.

2. Sleep physiology and polysomnogram, physiopathology and symptomatology in sleep medicine

2.1 Sleep physiology and polysomnogram in sleep medicine

Sleep is a physiological and behavioral process that an individual requires to carry out his daily functions. This process is completed in a regular and continuous manner every night. As a part of biological rhythm, human brain has a healthy functioning by differentiating dark and day hours of the day. From controlling hormone levels to muscle tone, from regulating pace of breathing to contents of our thought; sleep influences all bodily and mental functions. It is not surprising that sleep can make these changes happen in the body because sleep causes significant changes in the electrical activity of the brain as a whole [1]. Sleep characterizes itself by not responding to one's surroundings and by drifting away from perception; yet it is a reversible behavior. During 1940–1950, physiologists believed that sleep was initiated as a result of tiredness that developed during the day and by a slowing down in the activation of the fore brain from

weakening in the activation of the reticular activating system. Later, based on transection studies, brain stem was shown to be responsible for generating sleep especially studies in cats; where total sections performed on pontine tegmentum induce sleeplessness. Physiologist Nathaniel Kleitman was working at Chicago University and he discovered REM sleep together with his colleague Dement in 1959 leading to a revolution in the field of sleep medicine. Two colleagues demonstrated the nature of sleep and the relation of eye movements with sleep by recording spontaneous whole night sleep. During their observations, it was understood for the first time that sleep consisted of 90–120 minutes cycles, it first got deep and then became superficial, and that during this superficial stage rapid eye movements appeared and then sleep deepened once again. Through the same series of observations it was found that, during the first half of the night deep sleep was more frequent and that REM sleep constituted 20–25% of the total length of the sleep [2, 3]. Sleep has an important function in an individual and sleep deprivation for a couple of days can hinder an individual's cognitive and physical performance, general productivity and health. The vital role of sleep on homeostasis can be clearly demonstrated by the possible death of rats who suffer from sleep deprivation for 2–3 weeks. Despite the obvious importance of sleep, we still have limited information about why it is an obligatory part of life. Sleep has two main types of physiological effects: First, its effect on the nervous system itself and second its effects on other functional systems of the body. There is no doubt that the effects on the nervous system are important. Long lasting wakefulness generally leads to progressive impairments of thought processes and even to abnormal behavioral activities (thoughts are blurred, as the duration of wakefulness lengthens irritability and psychosis ensues). Therefore, sleep is considered to protect the normal order of brain activity by different means and to preserve the normal "balance" between the different functions of the central nervous system [4, 14].

2.1.1 Mechanisms of wakefulness and sleep

In the regulation of wakefulness and sleep brain stem, hypothalamus, basal fore brain and their neurotransmitters all play a role. When we analyze *the neuroanatomy of wakefulness and sleep*, we mainly see that neurons activating wakefulness and sleep are located at pontis oralis, mesencephalic central tegmentum, posterior hypothalamus and midline brain stem, dorsolateral medulla reticular formation and anterior hypothalamic-preoptic fields at different concentrations and different localizations. *Brain stem and reticular formation* are important anatomic localizations. Wakefulness is managed by reticular activating system (RAS). RAS is localized in the pons and midbrain. RAS stimulates the cortex by ventral and dorsal tracts. Ventral tract stimulates the frontal parts of the brain through hypothalamus and subthalamus, dorsal tract stimulates the cortex through the nucleus groups in the thalamus. During wakefulness transmission of sensory information from thalamus is permitted through RAS control managed by thalamus. During sleep, the activity of RAS stops and the transmission of sensory information through thalamus is blocked and the stimulation of cortex is prevented. *Anatomic structures responsible for the hypothalamic control of sleep and wakefulness*: for wakefulness, stimuli originating from rostral pons and caudal midbrain regions reach paramedian midbrain in diencephalon and here the signals divide into two paths aiming to reach thalamus and hypothalamus. Main structures projecting to thalamus are PedunculoPontine Tegmental (PPT) and LateroDorsal Tegmental (LDT) nuclei

that are of cholinergic nature. The structure that initiates sleep is thought to be the ventrolateral preoptic nucleus (VLPO) located on the anterior part of the hypothalamus. VLPO nucleus suppresses the activities of brain stem, pons and locus coeruleus, dorsal raphe nucleus, laterodorsal tegmental pedunculopontine tegmental nucleus via GABA and galanin neurotransmitters. *Suprachiasmatic Nucleus (SCN)* is known as the light sensitive circadian pacemaker. Throughout daytime light stimulus is transmitted from retina to hypothalamus through neural pathways and results in secretion of melatonin from the pineal gland. It is an anatomical structure that has a central role in maintaining the day-night rhythm [3–5, 10]. Neurotransmitters controlling sleep and wakefulness can be listed as: "Glutamate, Acetylcholine, Histamine, Norepinephrine and GABA". Reticular activating system stimulates the cortex by using glutamate while ponto-mesencephalic tegmental neurons do the same job by using acetylcholine. Neurons at locus coeruleus use mostly norepinephrine, these extend from the brain stem to the cerebral cortex by including the fore brain, and they activate the stimulation of the cortex and contribute to maintaining sleep. Cholinergic neuronal network results in wakefulness in two types of cortexes: (1) It projects to laterodorsal tegmental and pedunculopontine tegmental nuclei, midline and intralaminar thalamic nuclei and to a lesser degree to lateral hypothalamus and basal for brain. (2) Cholinergic neuron group starts from the basal for brain and has a widespread projection to cortex. This pontomesencephalic neuron group is part of the ascending reticular activating system; they not only play a part in the activation during wakefulness but also are actively involved in paradoxical sleep. Glutamate is another excitatory neurotransmitter; it acts as the primary neurotransmitter of the ascending reticular activating system. Glutamate is found at a very high concentration at the brain stem reticular formation. This neurotransmitter plays an active role in the wakeful brain and is secreted from the cortical cells to a significant degree throughout wakefulness. During slow wave sleep "burst discharges" appear due to the activation of special glutamate receptors. Histamine also plays an important role in wakefulness. Neurons containing histamine are found in tuberomammillary nuclei and in posterior hypothalamus. Noradrenergic neurons (locus coeruleus), have diffuse projections in the brain that extend to the cortex. Histaminergic neurons are associated with cortical activation during wakefulness whereas they are shut down during REM sleep. To sleep there needs to be a shift from sympathetic regulation to parasympathetic regulation. Parasympathetic centers of significance are found in "solitary tract nucleus neurons, anterior hypothalamus and preoptic fields". Serotonergic raphe neurons facilitate the initiation of sleep while GABA-ergic neurons inhibit the activating system. These GABA-ergic neurons are selectively activated during slow wave sleep. As a result of this inhibition, brain stem, hypothalamus and nasal fore brain are suppressed and disfacilitation (inhibition) and hyperpolarization of thalamocortical system takes place. Thereby from the wakeful state where we see rapid, tonic discharges on EEG, the system shifts to sleep state we start recording sleep spindles and slow wave activity. Initiation and continuation of slow wave sleep is made possible by lengthening and strengthening the inhibition of the activating system with GABA-ergic system [1, 4–11].

2.1.2 Normal sleep

Sleep is a complex mix of physiological and behavioral processes. Typically, sleep takes place while the individual is in a horizontal position, immobile with closed eyes and when all other indicators point out to sleep. There are two

distinct stages of sleep: The one with non-rapid eye movements (NREM) and the one with rapid eye movements (REM). These stages are differentiated from one another and from wakefulness with clear margins. NREM sleep is classically divided into three stages based on EEG. EEG patterns usually consist of a mixture of synchronous sleep spindles, regular waves like K-complexes and high voltage slow waves. Based on the depth of sleep, there are three NREM stages, during the first two stages, wake-up thresholds are generally low and during the third stage it is at its highest or a body that can move and for a brain that can regulate, NREM sleep is a relatively inactive state going together with minimal and fragmental activity. On the other hand, during REM stage, the body is immobile because of muscular atonia, in EEG shows activation and episodic rapid eye movements can be observed. Sleep cycle starts with NREM (calm, synchronized sleep, deep wave sleep); nearly every 90 minutes NREM and REM (mobile, desynchronized, paradoxical sleep) follow one another. Slow wave sleep dominates the first one third of the night and is related to the duration of wakefulness before sleep. REM sleep dominates the last one-third portion of the night and is related to the circadian rhythm. First stage of sleep, namely NREM-1 lasts only for a couple of minutes after the initiation of sleep and it goes together with low wake-up threshold and provides the transition from wakefulness to sleep. NREM-2 stage of sleep is identified by the presence of sleep spindles and K-complexes on EEG. To wake-up, there needs to be a more intense stimulus during NREM-2 compared to NREM-1. If stimuli given during NREM-1 are administered during NREM-2, there is no arousal; but K-complexes will appear. NREM-2 gradually progresses to high voltage slow activity and transforms into NREM-3 stage. In a young healthy individual, the percentage of slow waves in sleep pattern should be 20–50%. NREM-REM cycles of sleep follow throughout the night by repetitions. First NREM-REM cycle lasts about 70–100 minutes, the second and further cycles last around 90–120 minutes. In young adults, during the first one third of the night deep sleep is predominantly seen during NREM stage, whereas during the last one-third portion of the night REM sleep dominates. Short wake-up periods usually happen when shifting to REM sleep [10, 11].

2.1.3 Electrophysiological signal recordings of wakefulness and sleep

During wakefulness electroencephalogram (EEG) reflects an active cerebral cortex engaged in perception and cognitive functions that shows relatively low voltage, high frequency and rapid activity. The discharge by a single neuron or a single nerve fiber can never be recorded from the scalp surface. Only when thousands even millions of neurons or fibers are simultaneously fired, electrical potentials pertaining to a single neuron or a single fiber can be recorded as this much of an electrical potential would suffice to make such a measurement from scalp surface [1]. When eyes are closed, several neurons show synchronous discharges at a frequency of 12 per second constituting alpha waves. When the eyes are opened afterwards, the activity of the brain increases to a greater degree; but the synchronicity of the signals decrease which leads to the canceling out of the brain waves. As a result of this, weak waves of higher but irregular frequency which are called beta waves appear. If the cortex does not have any connection with the thalamus, then alpha waves are not generated. Stimulation of non-specific reticular nuclei that surround thalamus and stimulation of diffuse nuclei that are located inside the thalamus result in the generation of waves in the thalamocortical system with a frequency of 8–13 per second which is the natural frequency for

alpha waves. That is why it is possible that alpha waves appear from the spontaneous negative feedback impulses in the diffuse thalamocortical system that also includes brain stem activating system. Delta waves include all the waves in EEG that have a frequency of less than 3–5 per second. They appear during very deep sleep, they also appear in the experimental animal studies where cortex has been separated from the thalamus with a subcortical section. Therefore, delta waves can appear in the cortex independent of the activities in the lower parts of the brain. Sleep spindles are produced by the thalamus. They appear as 12–15 Hz oscillations in between slow waves during NREM sleep in human EEGs. The production mechanism of these oscillations is related to the degree of hyperpolarization in thalamocortical cells. While shifting from wakefulness to sleep, the membrane potentials of thalamocortical cells are exposed to a progressive hyperpolarization, thus synaptic responsiveness decreases and sensory information transfer is prevented. When a sufficient level of hyperpolarization is achieved, we start seeing rhythmic bursting in nucleus reticularis neurons belonging to thalamus at a frequency interval which is in correlation with sleep spindle. Furthermore, slow wave oscillations due to membrane hyperpolarization also take place. It is accepted that sleep homeostasis is significantly affected by the size and characteristics of the sleep spindles that are formed [11–14].

2.1.4 Polysomnogram and polysomnography

"Polysomnography" "PSG" is the recording of sleep via electrophysiological signals. Sleep recordings that appear on a sheet of paper or on a computer screen are called "Polysomnogram". Throughout one night electrophysiological signals recorded during wakefulness and sleep are as follows: "Electroencephalogram (EEG), electromyogram (EMG; jaw, arm and leg), electrooculogram (EOG), electrocardiogram (ECG), snoring, oro-nasal air flow (L/s) (liter/second) chest and abdomen movements (respiratory effort recordings), O_2 saturation, and body position and real time-video-image recordings". "Penile tumescence, gastroesophageal reflux and blood pressure" are other electrophysiological signals that are recorded, despite not being performed for all patients. Polysomnography is the procedure where different physiological or pathophysiological parameters are recorded during sleep for six or more hours, evaluation of these by a medical doctor and generation of a report (**Figure 1**).

Polysomnography is performed for two main purposes: (1) Understanding physiological (normal) sleep and meanwhile demonstrating the changes that take place in the organism (for example heart rate changes can be analyzed)

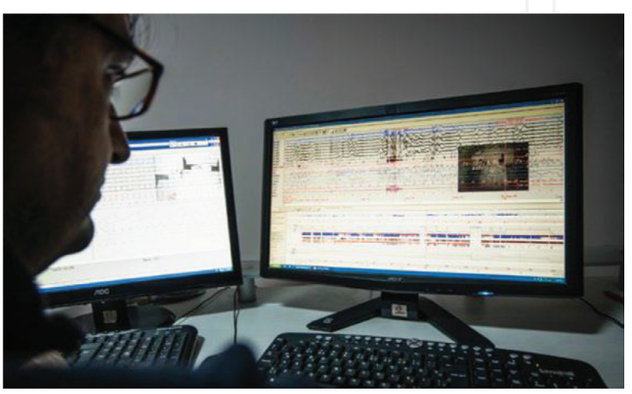

Figure 1.
Examination of a polysomnogram by a medical doctor.

(2) Identification of abnormal events that take place during sleep; diagnosis of different sleep disturbances, guide in their treatments. PSG starts by explaining the procedure to the patient in great detail. The patient should understand that there would not be any pain involved with the procedure, that no medications would be used. The patients are informed that their natural sleep will be recorded through superficial electrodes to be placed on their bodies. The patients should be reminded that they would not be spending the night by themselves, and that a technician would be present to follow the process from a monitor. After the patient puts on his sleepwear, electrodes are placed for an overnight sleep test and calibration process is initiated. First, the calibration of PSG equipment is made. This is performed before the electrodes are placed. Afterwards the electrodes are calibrated. This is done after the electrodes are placed in the electrode box. Lastly, physiological calibration is performed. This calibration is performed via the electrodes that transmit physiological changes through EEG, EOG, and EMG, leg movements, chest and abdomen movements. The PSG records of electrophysiological signals features are as follows (**Figure 2**): *EEG recordings during PSG*: Gold and silver electrodes are used for sleep EEG. It is important to clean the skin where the electrodes are to be placed. This is performed to decrease the resistance between the skin and the electrodes. Another important issue is to use substances that would increase the conductivity of the electrodes and to make sure that electrodes stay in place

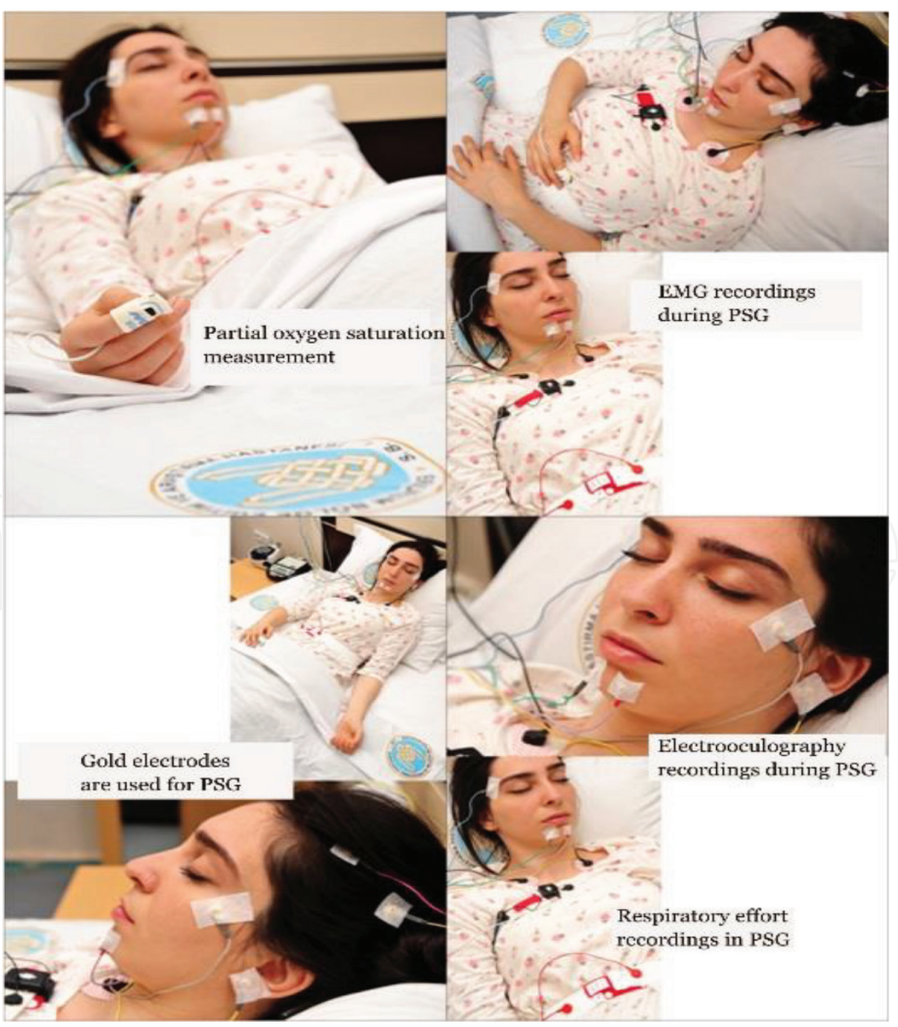

Figure 2.
The PSG records of electrophysiological signals.

throughout the night. Most commonly used fixer is "collodium". For PSG, it is recommended to have recordings from at least three channels. These channels are F4-M1, C4-M1 and O2-M1. M1 is placed on the left mastoid process. To these electrodes, F3, C3, O1 and M2 electrodes are attached as back up. If one of the electrodes mentioned above gets bad during the night, then F3-M2, C3-M2 and O1-M2 derivations are used. Here, M2 corresponds to the right mastoid process. Additionally, Fz-Cz, Cz-Oz and C4-M1 derivations can be used for EEG recordings. For this spare electrodes Fpz, C3, O1 and M2 need to be placed. *EOG recordings during PSG*: The objective of having electrooculography recordings during polysomnography is to identify the eye movements. This recording is in fact the recording of the voltage difference between cornea and retina. With the movement of the eye, the distance from the retina and cornea to the electrodes changes and creates a dipole. This change is recorded with EEG. Two EOG electrodes are used in PSG recordings. E1 is located 1 cm below the left lateral canthus E2 is placed 1 cm above the right lateral canthus. Both electrodes are referred to the electrode (M2) placed on the left mastoid process. That means EOG is recorded from two channels as E1-M2 and E2-M2. Alternatively, E1-Fpz and E2-Fpz can be used. *EMG recordings during PSG*: In polysomnography, electromyography (EMG) is of importance in detecting R stage (REM sleep). This recording is different than a classical EMG. It is performed to assess striated muscle tone. Using three electrodes is recommended for this recording; only two of these are used to do the recording. Superficial electrode is placed on the mandible and is referred to either of the electrodes placed below this. In polysomnography it is sufficient to have only one channel for EMG recording. *Respiratory Effort Recordings in PSG*: In polysomnography, there needs to be at least three respiratory parameters recorded: "oro-nasal air flow (L/s) chest and abdomen movements and O_2 saturation". Recording of stopping air flow (apnea) is performed by oronasal thermal sensors. For the recording of respiratory effort, inductance plethysmography method is used. For the measurement of O_2 saturation, pulse oximetry that identifies the O_2 saturation of hemoglobin in the capillary blood would be the most appropriate method. *Recording of Periodical Leg Movements (PLM) during Sleep in PSG*: Superficial electrodes are placed on the anterior tibial muscle. Two electrodes should be placed to each leg (active, passive) and one channel should be recorded from each leg adding up to two channels. Peak to peak amplitude of the EMG activity that is generated in the absence of movement should be 4–6 microvolts, at least four movements should take place with 5–90 seconds intervals and each of these movements should take 0.5–5 seconds to fulfill the criteria for PSG diagnosis of periodic limb movement disorder. *Multiple Sleep Latency Test-MSLT*: This is the electrophysiological signal recording method used to objectively evaluate daytime sleepiness. This is a polysomnographic recording obtained during daytime and a half to 3 hours after waking up from a nocturnal polysomnogram. It should consist of five tests of 20 minutes duration, which are 2 hours apart from each other. Two basic data for evaluation: (1) Time of sleep onset (2) Appearance of REM sleep throughout the recording process. REM of short duration that appears during recording is defined as SOREM (Sleep Onset REM). MSLT; is part of the clinical evaluation for narcolepsy and idiopathic hypersomnia.

2.1.5 Recording and scoring of sleep

Scoring of sleep corresponds to staging of sleep. For the staging of sleep polysomnography recordings are separated into 30 second-long intervals (epoch); each epoch

is scored with a sleep stage. Sleep stages are as follows: "Stage N1 (or NREM1), Stage N2 (or nREM2), Stage N3 (or NREM3), Stage R (REM), Stage W (wakefulness)". Each 30 second interval needs to match with one of these stages. Three main electrophysiological signals are used when sleep stages are identified: "EEG, EMG, EOG". There three parameters are evaluated for each epoch and one sleep stage is matched with each 30 second interval. There are certain rules to be respected when staging of sleep is performed: *Stage N1*: it is generally regarded as the stage where the shift from wakefulness to sleep happens (sleep initiation stage). If more than one half of an epoch consists of low amplitude and mixed frequency EEG activity that replaces alpha rhythm, this part is staged as Stage N1. In an individual who does not have any alpha activity during wakefulness, seeing only one of the following three features in EEG is sufficient to categorize that part as Stage N1: (1) Baseline activity in EEG should be at least 1 Hz lower than that is seen during wakefulness. (2) Observing sharp vertex waves on EEG (in central regions with duration of shorter than 500 ms, waves with sharp edges). (3) Slow eye movements should appear in EOG (lasting longer than 500 ms, conjugated, regular, and sinusoidal) (**Figure 3**). *Stage N2*: it is the longest portion of sleep both in terms of duration and proportion. In EEG, the presence of either a sleep spindle or K-complex results in naming that stage as Stage N2 (**Figure 4**). Stage N2 sleep starts in this manner and despite the absence of K complex and/or sleep spindles, the stage continues being N2 until further changes take place in the epoch (Stage W, N3, R or arousals). Only when there is a progress to Stage W, Stage 3 or Stage R or when an arousal appears, Stage N2 is concluded. *Stage N3*: It is called as slow wave sleep. In EEG, it is seen as delta activity with a frequency of 0.5–2 Hz and with amplitude that is more than 75 microvolts. During this stage there can be sleep spindles and K complexes. The only criterion for Stage N3 is the presence of slow waves (delta wave oscillations) in more than 20% of this part (**Figure 5**). *Stage R*: indicates REM sleep. In terms of central nervous system functioning this is a completely different stage of sleep. Three features are required in the epoch to be called Stage R (1). In EEG the wave activity is of low amplitude

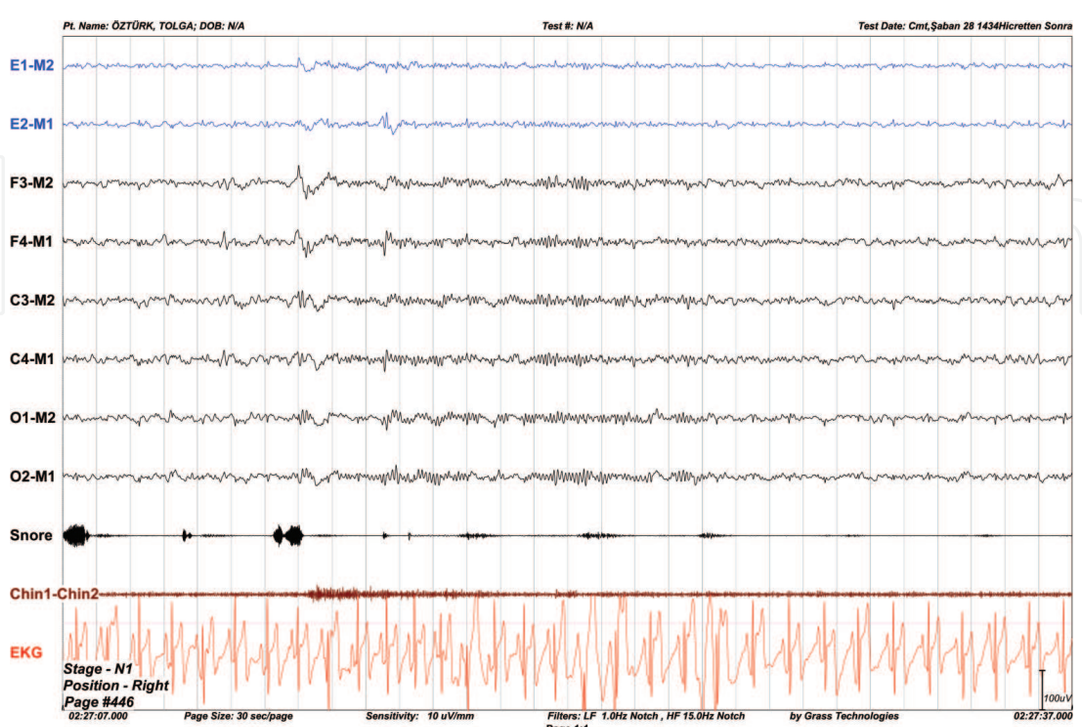

Figure 3.
Stage-N1.

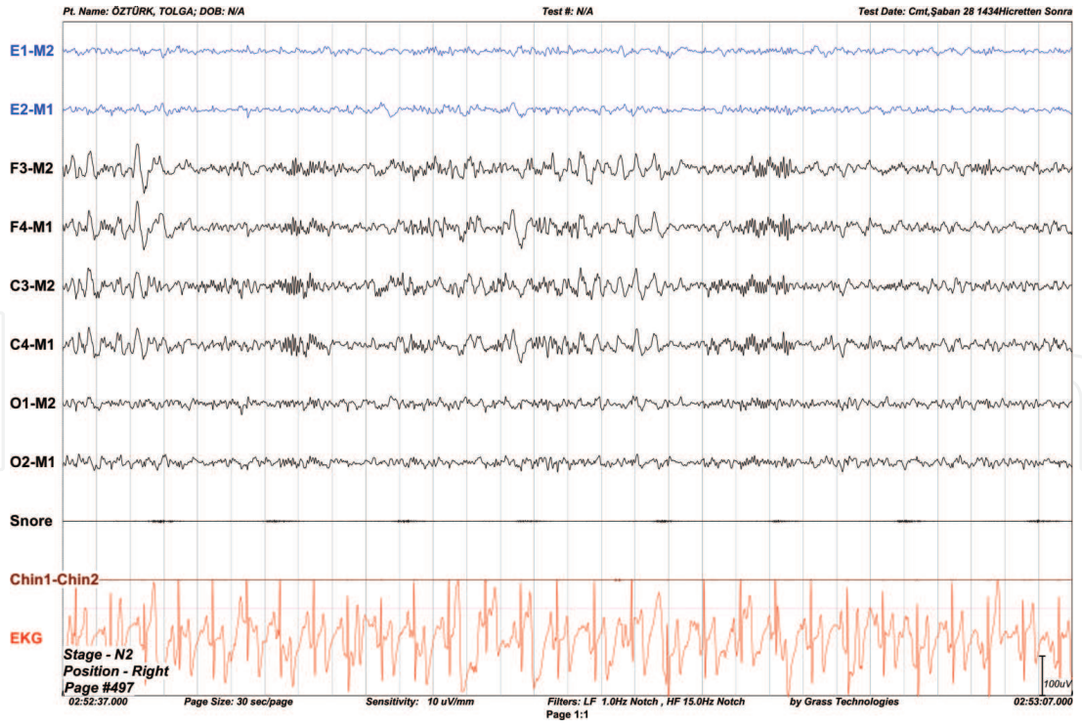

Figure 4.
Stage-N2.

and mixed frequency (2). In jaw EMG, there is a low basal EMG activity which is the lowest of all stages (3) In EOG rapid eye movements are observed (rapid eye movements—REM; these are eye movement shorter than 500 ms in duration, when are conjugate, irregular, sharp spike eye movements). In epochs that follow Stage R, even in the absence of rapid eye movements, if the other two rules remains, it continues to be classified as Stage R (**Figure 6**).

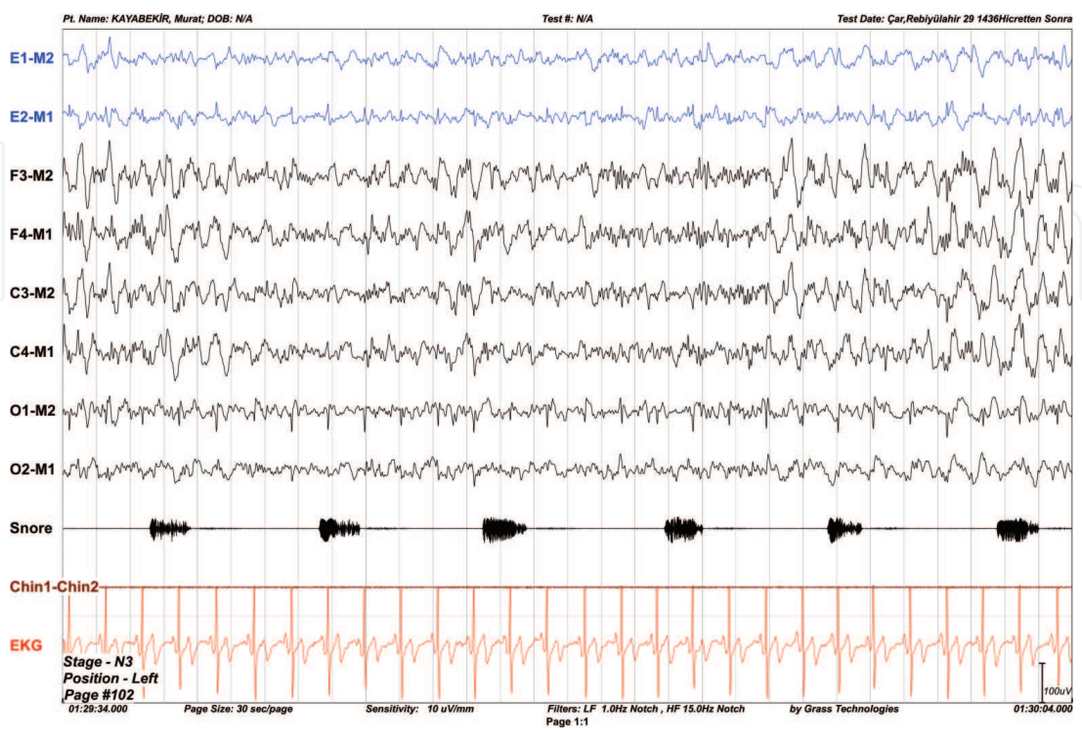

Figure 5.
Stage-N3.

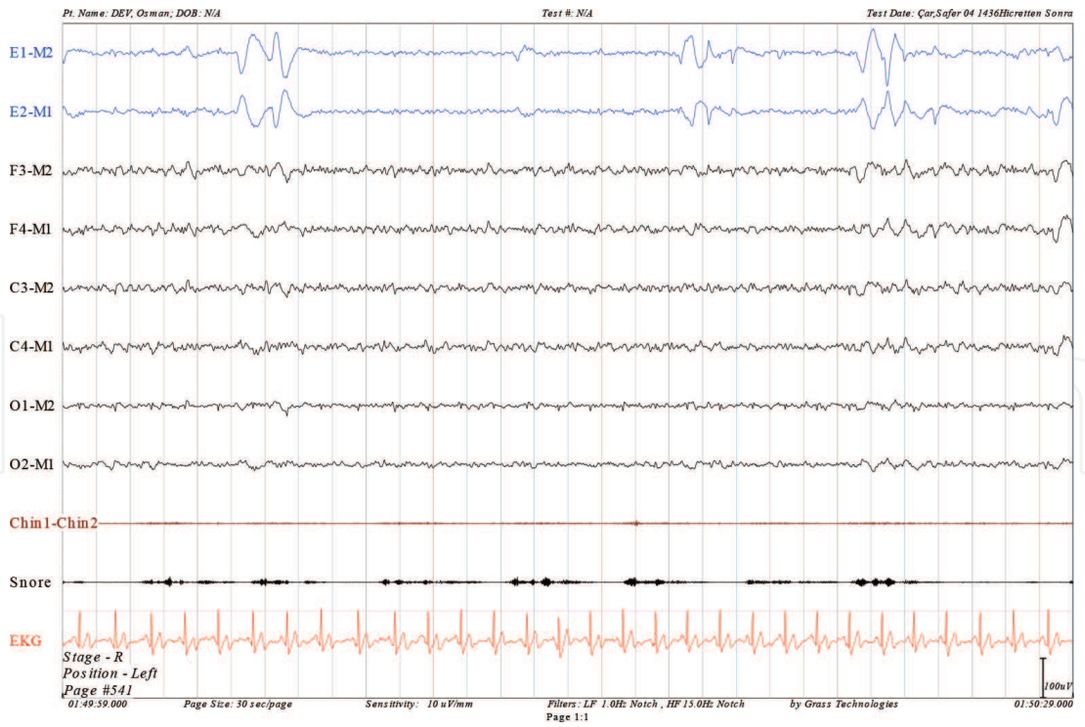

Figure 6.
REM sleep.

2.1.6 Recording and scoring of breathing during sleep

American Academy of Sleep Medicine (AASM) has published the rules for scoring sleep, sleep associated events as well as respiratory events. Based on these rules, abnormal respiratory occurrences that are observed during sleep are "apnea, hypopnea, arousal associated with respiratory effort, hypoventilation and Cheyne-Stokes breathing". Electrophysiological signal recordings that are required for interpreting respiratory problems in PSG are: "O_2 saturation, nasal/oronasal air flow (nasal cannula, thermistor), thoracic, abdominal respiratory effort, EEG recordings (absolutely required to identify arousal), body position, tracheal microphone, ECG, leg EMG recordings". To detect respiratory effort the following methods are used: (1) *Measurement of thoracic and abdominal movements*, this is the most widespread method used in the sleep laboratories to detect the respiratory effort. (2) *Respiratory muscle EMG*, standard electrodes are placed into intercostal spaces. These can be mixed with ECG recordings. This is the oldest method available. (3) *Pleural pressure*, esophageal pressure is measured to measure the inspiratory effort. Patients cannot tolerate esophageal balloons. Newer, thin, piezoelectric transducers with catheter tips are better tolerated. Esophageal pressure measurements are very helpful in two instances: (a) Identification of central apnea and hypopnea with a high sensitivity (b) The diagnosis of upper respiratory tract resistance syndrome. However this method is uncomfortable.

Apnea scoring: Apnea starts with a net loss of breathing amplitude when signals coming from nasal cannula as an alternative to oronasal thermistor stops and it ends with the start of the first breath that comes close to the basal value. Apnea is scored based on the following criteria: (1) 90% or more of a decrease in the peak signal of the thermal sensor compared to the basal amplitude. (2) Having an incident of at least 10 seconds duration. (3) At least 90% of the incident fulfilling the amplitude decrease criteria required for apnea scoring.

Based on respiratory effort, there are three types of apnea: (1) Obstructive apnea: apnea during a respiratory effort. (2) Central apnea: apnea criteria and the absence of respiratory effort during the period where air flow stops. (3) Mixed apnea: apnea criteria that start with an absence of respiratory effort and follows with a continuing increase in respiratory effort. *Hypopnea scoring*: It is performed based on following criteria: (1) More than 30% of a decrease in the signal amplitude of the nasal cannula compared to the baseline. (2) The episode lasting for at least 10 seconds. (3) 4% or more of a decrease in the O_2 saturation compared to the baseline saturation. (4) At least 90% of the incident should satisfy the amplitude decrease parameters accepted for hypopnea. *Apnea index (AI)*: defines the number of apneas that occur within an hour while sleeping. *Apnea-hypopnea index (AHI)*: defines the total number of apneas and hypopneas combined during an hour while sleeping. *Respiratory effort related arousal (RERA) scoring*: arousal resulting from 10 seconds or longer of flattening of the inspiratory portion of nasal pressure which does not fulfill the criteria for hypopnea or apnea. *Respiratory disturbance index (RDI)*: it defines the summation of apnea, hypopnea and RERA incidents that appear in an hour during sleep. *Hypoventilation scoring*: if $PaCO_2$ increases more than 10 mmHg during sleep compared to levels obtained in supine position during wakefulness this is scored as hypoventilation. *Cheyne-Stokes breathing is score*: when there are at least three consecutive crescendo and decrescendo breathing changes, with at least one of the following criteria: (1) five or more central apnea or hypopnea during an hour of sleep (2) breathing amplitude changes in crescendo-decrescendo style in a consecutive manner lasting at least 10 minutes (3) Cheyne-Stokes breathing cycle lasting for 60 seconds in general, but variable. *O_2 saturation measurement*: measurement of O_2 saturation is generally performed with pulse oximetry. It detects the O_2 saturation of hemoglobin in the capillary blood through the emission and absorption of light generated from a source. *O_2 desaturation index (ODI)*: it defines the number of oxyhemoglobin desaturation incidents per hour seen during sleep [15–18].

2.2 Physiopathology and symptomatology in sleep medicine

2.2.1 Relationship of sleep with body systems and diseases

Cardiovascular system: known hemodynamic measurements "heart rate, heart rate variations, blood pressure, cardiac output, baroreflex activity and peripheral vascular resistance" provides us important information as to how the cardiovascular system functions in sleep as well as in wakefulness. In NREM and REM stages of sleep, due to parasympathetic system activation heart rate, blood pressure, cardiac output and peripheral vascular resistance decreases. Lowest levels of arterial blood pressure are seen during Stage N3. The decrease in the heart rate is related to the decrease in the sympathetic motor tone. During NREM sleep; blood pressure, respiratory rate and basal metabolic rate decrease by 10–30%, this is the most comforting and most restful period of deep sleep. In the hemodynamic changes in sleep, arterial baroreflex mechanism is thought to play a regulating role. Baroreflex arch consists of peripheral receptors (sinus caroticus and arcus aorta), central neurons (tractus solitorius and medulla oblongata) and afferent and efferent (sympathetic, parasympathetic) neurons. The decrease in blood pressure is compensated with an increase in the heart rate centrally through this reflex arch, or vice versa. From a cardiovascular perspective, during NREM sleep, there is relative autonomic stability, sympathetic inhibition, and increase of vagal (parasympathetic) tone. It is also the stage where bradycardia

and respiratory sinus arrhythmia is seen. Despite the fact that there is parasympathetic predominance during REM sleep, due to bursting in sympathetic nervous system, blood pressure increases and variations are observed in the heart rate. During this stage, first degree or Wenckebach type second degree AV blocks, and sinus blockage can take place due to increased vagal tone. During Stage N3 blood pressure decreases by 10–20% and heart rate by 5–10% (dipper). The absence of the expected nocturnal decrease in blood pressure is called non-dipper, while a decrease of extreme scale is called extreme dipper and both can lead to cardiovascular events. Compared to NREM, blood pressure is higher during REM sleep; myocardial infarction, unstable angina, cardiac death, ventricular tachyarrhythmias, pulmonary embolism, cerebrovascular incidents and sudden cardiac death can take place during REM stage of sleep that intensifies during early hours of the day during which there is autonomic instability (sudden sympathetic discharge) triggering platelet aggregation, plaque rupture and coronary spasm [19–25]. *Respiratory system*: control mechanisms for respiration during sleep: (1) homeostatic and metabolic control; O_2 and CO_2 sensitivity mechanisms on carotid bodies through chemoreceptors provide for the regularity of breathing. (2) Behavioral (cortical) control; during activities like speaking or swallowing breathing is controlled voluntarily. (3) Wakefulness warning; during wakefulness reticular activating system sends non-tonic stimuli to the respiratory center in the brain stem resulting in an increase in breathing. NREM and REM stages are controlled with metabolic stimuli. It is shown that respiratory response by chemoreceptors decreases during NREM and this decrease gets more significant during REM. The main stimulus for respiration is $PaCO_2$, the effector organ is the lungs, and the chemoreceptors that regulate the response to stimuli are located on carotid bodies and brain stem. The system operates with stimuli and feedback mechanisms. For example, during heart failure the response to stimulus is delayed as a result of lengthened circulatory time. Likewise, a minor change in ventilation can result in a significant change in CO_2 and can cause impairment in respiratory balance. Instances where the tendency to central apnea increases in the organism are: (1) During transition to sleep; when CO_2 is at a level that is lower than that is required to stimulate respiration and the number of respiration becomes insufficient. (2) When the ratio between respiratory response and respiratory stimuli is high; idiopathic sleep apnea is an example for this. (3) Lengthened circulatory time; for example during cardiac failure typically Cheyne-Stokes breathing develops. (4) Instances where respiratory control gets out of order; in conditions pertaining to the brain, in patients with decreased or disappeared chemosensitivity, hypercapnia is seen during wakefulness. These patients experience hypoventilation especially during REM stage. That is why in patients having central alveolar hypoventilation and obesity hypoventilation syndrome, the ventilation is further hindered during sleep; so hypoxia, hypercapnia, both central and obstructive apneas are observed [26–30]. *Upper respiratory tract*: it is a multipurpose conduit. As it allows for the passage of liquids and food, it is where activities like talking, swallowing and breathing take place. It contains the following structures: "Extrathoracic trachea, larynx, pharynx and nose". The segment with the highest tendency to collapse in the respiratory system is the pharynx. The pharynx consists of three parts: (1) Nasopharynx is the part that extends from the nasal passage to the hard palate. (2) Oropharynx is divided into two parts as retropalatal and retroglossal fields. (3) Hypopharynx starts from the root of the tongue and extends to the larynx. In most of the patients with Obstructive Sleep Apnea Syndrome (OSAS), narrowing or closure of the airways that happen throughout the sleep takes place in the retropalatal and retroglossal region. For the preservation of the patency of the upper airways,

two important physiological mechanisms need to be in balance: (a) Forces that cause the collapse of the pharyngeal airways (the amount of soft tissue that covers the airways and the size of the airways). (b) Forces that dilate the pharyngeal airways (the activity of a muscle group that work in a coordinated manner to keep the airways open). Predisposing factors that would impair this balance are: "Mainly age and gender and then race, obesity, neck circumference, cigarette-alcohol-sedative use, genetic factors, co-morbid diseases (acromegaly, hypothyroidism, Down Syndrome, storage diseases like amyloidosis and mucopolysaccharidosis), body posture and gravity, anatomic factors, genetic factors and hormones influence the patency of upper airways and constitute the risk factors for OSAS [31–35]. *Sleep and immune system*: among the substances that are both sleep inducing and immunologically active we can list; Interleukin-1 (IL-1), IL-2, alpha interferon, Factor-S, muramyl peptides, tumor necrosis factor (TNF) and prostaglandin D2 (PGD2). We know that people who are sleep deprived can get sick more easily and when they pay attention to sleeping properly and resting, they heal faster. Several factors play a role in sleep regulation. TNF-alpha, IL-1-beta, growth hormone releasing hormone (GHRH), PGD2 and adenosine affect NREM sleep, whereas vasoactive intestinal peptide (VIP), nitric oxide (NO) and prolactin exert their effects on REM sleep. In the regulation of sleep-wakefulness, elements of immune system that are of significant value are; IL-1, IL-6 and TNF. When the endogenous production of IL-1-beta and TNF-alpha increases (overnutrition, infectious disease states) NREM sleep increases. The effects of certain cytokines on sleep can be summarized as follows: *Prosomnogenic cytokines*: IL-1-beta, IL-1-alpha, TNF-alpha, IL-2, IL-6, IL-15, IL-18, epidermal growth factor, nerve growth factor, interferon-gamma, neurotrophins nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophin 3, and 4 have been observed in elevated concentrations in allergic diseases, and they cause swelling and tenderness in the joints, and increase the tendency for autoimmune diseases like rheumatoid arthritis. The secretion of such factors by the immune system peaks during the early hours of the night and with gradual decreases they reach their lowest levels during morning hours. Short term sleep deprivation lead to decreases in natural killer (NK) cell activity, when this deprivation lasts longer there is an increase in NK cell activity. Experimental studies on laboratory animals have shown that, in instances of lengthened sleep deprivation fatal bacterial infections stemming from the gastrointestinal system can turn fatal within 3 days. In narcolepsy cases increases have been observed in TNF-alpha levels. In OSAS patients the circadian rhythm of secretion for TNF-alpha deteriorates significantly [36–40]. *Endocrine Physiology during Sleep*: Circadian rhythm and homeostatic balance provide for the control of hormonal and metabolic changes during sleep. Sleep deprivation studies analyze the effects of sleep and circadian rhythm on hormones. Based on these studies, growth hormone (GH) and prolactin (PRL) secretion increases during normal sleep, cortisol and thyroid stimulating hormone (TSH) secretions decrease. If sleep is interrupted by wakefulness, GH and PRL decrease while TSH and cortisol increase. Physiologically cortisol decreases starting from early hours of the morning towards the evening by reaching its lowest levels during the late hours of the day and initial hours of sleep. A couple of hours before waking up, there are reactivation of cortisol secretion. Low levels of cortisol is associated with slow wave sleep. During sleep deprivation the amplitude of cortisol rhythm decreases 15% compared to normal. Especially in elderly individuals who have fragmented sleep patterns, as deep sleep decreases as well, there is an increase in cortisol levels during night time and this is associated with decreased memory and increases in insulin resistance. In Cushing syndrome patients, due to bad

sleep quality decreases have been shown in REM latency, increases in first REM intensity and decreases of deep sleep. There are three basic processes coming into play in sleep regulation: (1) Homeostatic process: it tells us the relationship between last sleep and wakefulness periods. Sleep deprivation in the organism increases the duration and depth of sleep as a compensatory mechanism. (2) Circadian process: it is also defined as the biological clock. (3) Ultradian process: it defines the duration of REM—NREM sleep cycles and the interactions between them. Melatonin is the neuroendocrine modulator of day-night rhythm. Melatonin receptors are densely located at the suprachiasmatic nucleus (SCN). The endogenous circadian rhythm of melatonin secretion is in parallel to the endogenous rhythm of sleep tendency. Secretion of melatonin from the pineal gland is under the control of SCN. This pathway is multisynaptic and has contributions from the sympathetic nervous system. Melatonin has three important physiological features: (1) Hypnotic effect: the ability to initiate sleep when homeostatic effect is inadequate to initiate or to maintain sleep. (2) Chronohypnotic effect: it is the ability to inhibit the time of waking-up that is normally regulated by the circadian center. (3) Chronobiotic effect: concerning the regulation of the circadian rhythm, it is the ability to initiate phase shifts and to do this during desired hours. The light that an individual is exposed to during night hours causes sudden decreases in melatonin levels. Beta blockers used for the prophylaxis of hypertension, cardiac arrhythmias and headaches block the sympathetic activity both at the heart and at the pineal gland. On the other hand, antidepressant drug fluvoxamine prevents the degradation of melatonin and increases its plasma concentrations. Neurotransmitter imbalance has been shown to be present in SCN of essential hypertension patients and there is a decrease in the secretion of melatonin in coronary artery disease that follows. These findings bring forward the possibility of using melatonin in hypertensive patients. At the beginning of sleep norepinephrine and epinephrine levels decrease and they reach their lowest levels within an hour. In patients with OSAS there is an increase in the levels of nocturnal catecholamines. Despite long hours of fasting during sleep, blood glucose levels have been shown to remain stable. Leptin that plays an important role in energy balance by suppressing appetite (produced by adipose tissue), increases significantly during sleep at night and thus increases slow wave sleep. In lengthened sleep deprivation, there is suppression of the night increases of leptin [41–45]. *Gastrointestinal System*: Gastric acid secretion has a circadian rhythm. Basal acid secretion is at its lowest during the hours of the day where there is no food intake, while it is at its highest during midnight. In healthy individuals, there is no relationship between gastric acid secretion and the stages of sleep. Together with the inhibition of acid secretion throughout the night (with H_2 receptor blockers and proton pump inhibitors) the healing of duodenum ulcers could be shown. Small bowel and colon motility decrease during sleep. In studies conducted on patients with irritable bowel syndrome, significant lengthening of REM sleep was identified [46].

2.2.2 Basic signs in sleep disorders and pathophysiological causes (semiology, propedeutics, preliminary instruction, introduction to further study)

The first step in the evaluation of a patient with a sleep disorder is to identify the main symptom. A detailed history of the sleep and wakefulness cycle constitutes the second step. This is followed by the medical history of the patient, a list of previously used medications, family history, detailed information about school, work, family and social life and a physical exam of bodily systems. Relevant laboratory tests are performed for differential diagnosis.

PSG establishes the definitive diagnosis. Despite developments in the field of sleep medicine, we see that neither the society nor the physicians are adequately informed about sleep and sleep disturbances. However, diseases associated with sleep are frequent in the population and can have significant consequences: they can negatively influence the individual's "work or school success, social life, marriage and other relationships as well as leading to occupational and traffic accidents. Sleep disturbances can hinder the cognitive functions of an individual and can increase the risk of having psychiatric and other system related diseases. Sleep apnea syndrome has a role in the etiology of severe diseases namely hypertension, myocardial infarction, heart failure, stroke and diabetes. Sleep deprivation can result in an increase in the number of seizures in a patient with epilepsy. Complaints of patients with diseases of other systems can be related to sleep disorders: in a patient having a follow-up with a Holter recording for hypertension, the reason behind an increase in blood pressure during sleep can be sleep apnea syndrome. Frequent arousals during the night, chest pain, not being able to climb the stairs during the day, tiredness, complaints about sleepiness are evaluated as angina by cardiologists and angiograms are performed. However, a PSG to be performed on this patient can establish the correct diagnosis of central apnea syndrome. In a patient with goiter disease, during an overnight sleep test, it is possible to diagnose sinusal bradycardia. Likewise, patients having severe OSAS can have predominant depression symptoms and can therefore admit to psychiatry outpatient departments. Children admitting to pediatric neurology outpatient departments with sleep episodes are valuated multidimensionally and then treated for epilepsy. However, if these children were to undergo PSG and MSLT (multiple sleep latency test), correct diagnoses of underlying sleep apnea syndrome, central hypersomnia and narcolepsy could have been established.

Insomnia: it is described as "difficulty falling asleep or staying asleep"; short, inadequate, superficial, easily disruptable and non-restorative sleep. The amount of sleep an individual needs changes from one person to the other based on genetic traits. Some people carry out their daily functions with 5 hours of sleep a day, whereas others who do not sleep nine to 10 hours can feel bad the next day. Sleeplessness can be related to a primary disturbance related to mechanisms of sleep or can develop due to an underlying disease. Acute insomnia develops due to an abrupt change in environmental, physical or cognitive factors that initiate sleeplessness. Sleep complaints only disappear when the individual gets used to this new condition. There are different diseases underlying primary insomnia; circadian rhythm disturbances, drug-substance use or sudden discontinuation of their use. Acquisition of behavior that hinders sleep hygiene can result in chronic insomnia. Psychophysiological insomnia is learned insomnia; the patient starts getting tense as the time for going bed approaches. This effort to get asleep and tension cause a performance anxiety and ends up being the main reason of insomnia. As the patient searches for behavioral changes to relieve herself of this anxiety, insomnia becomes inextricable: inadequate sleep hygiene, night eating (drinking) syndrome, alcohol-hypnotic-stimulant related insomnia are examples to insomnia for which such behavioral changes and habits lay the foundation. Causes of pain that increase during the night that negatively affect sleep and trigger insomnia are: "entrapment neuropathies, cluster headaches, arthritis, rheumatic pain, pain and paresthesia of the legs that are seen before falling asleep in restless leg syndrome. Most of the psychiatric diseases have a relationship with sleep: "In depression and anxiety disorder, insomnia might have started years ahead and likewise insomnia might

foreshadow psychosis or manic episodes." Examinations of physical neurological and cognitive functioning of the patient might reveal important clues about insomnia. In anxiety, tachycardia, rapid breathing and cold hands; in sleep apnea syndrome, short and thick neck, obesity and narrow upper respiratory tract; in endocrine system pathologies hyperthyroidism characterized by excessive sweating and tachycardia, round face and buffalo hump in Cushing syndrome and neurological examination might reveal causes of insomnia like neuropathy and parkinsonism. It should be kept in mind that women with iron deficiency anemia may complain of insomnia. *Excessive sleepiness*: having somnolence at inappropriate times and in inappropriate environments and being unable to prevent it. Although somnolence might be related to the nature of the individual, to the wearisomeness of his daily life or to depression, it is an important symptom that forecasts sleep disorders. In its mild forms it is seen during rest, in advanced cases the patient might fall asleep during a conversation, while doing work, during eating or while driving. Hypersomnia leads to important work and traffic accidents. In differential diagnosis, daytime excessive sleepiness due to chronic sleep deprivation should be kept in mind; additionally, excessive sleepiness can be seen during heart, kidney and liver failure, rheumatic, endocrinological and neurological diseases. Slowing down of responses, frequent yawning, closing of the eye lids, hesitance during speech or movements are the physical signs for excessive sleepiness. In people with chronic hypersomnia, round dark circles underneath the eyes attract one's attention. Sleep disturbances where one can see hypersomnolence are: "sleep apnea syndrome, narcolepsy, idiopathic hypersomnia, parasomnias"; however, certain complaints that are obtained during history help in the differential diagnosis of these disease states. Such complaints are; "snoring, apnea episodes observed by close ones, morning headaches, nocturia, sleep paralysis, hypnogogic hallucinations, cataplexy and confusion while waking up from sleep". Idiopathic hypersomnia is characterized by increased sleep time and despite there is nothing that would hinder the quality of sleep, the individual feels himself sleepy which differentiates this condition from insomnia associated with sleep deprivation. *Tiredness*: patients who have excessive sleepiness also complain about tiredness and lack of energy. However, tiredness is not associated with tendency to fall asleep. Tiredness is an important symptom for many diseases. Especially in women, tiredness due to iron deficiency anemia is usually ignored and mostly confused with sleepiness and that is why women come to sleep laboratories. Endocrine and metabolic diseases, heart, kidney and liver failures and psychiatric conditions like depression can as well lead to tiredness and fatigue. *Snoring*: it is the sound generated during sleep due to the resonance of the tissues of the upper respiratory tract which is mostly heard during inspiration, rarely during expiration and sometimes during both phases. Due to narrowed upper respiratory tract the speed of the flowing air increases, this creates turbulence and increases the intensity of the sound. Patients are usually not aware of this and they are guided to a doctor by close ones who are bothered by the noise. Sometimes the patient wakes up with his own snoring or his own effort to breathe. Characteristic features of the snoring sound give clues as to whether the patient has sleep apnea or not. In patients who had undergone surgery for upper respiratory airways, apnea episodes might as well be seen in the absence of snoring. *Sleep apnea*: it is the stopping of respiration for 10 seconds or longer during sleep. The patient's partner or close ones describe it as an interruption of snoring, as patient holding his/her breath during sleep. During apnea the snoring stops, while the apnea ends the patient has a deep inhalation,

and the snoring restarts with a loud sound like roaring or snorting. These episodes can repeat hundreds of times through the night depending on the severity of the disease. The ending of apnea goes together with wakefulness reactions. This divides the sleep and hinders its quality. It might result in hypersomnia or insomnia. There are two main types of apnea: In central apnea air flow stops together with the effort of respiration. In obstructive apnea, air flow stops because of a narrowing in the upper respiratory tract but the effort of respiration still continues. Obstructive apnea is mainly accompanied by snoring and other complaints like night sweats, feeling of suffocation, nocturia, morning headaches, irritability, forgetfulness and depression and hypertension might follow. The patients are generally obese with short and thick necks; they also have narrow upper respiratory tracts. This body composition is not a rule though; people from all age groups including children might have obstructive apnea. Central apnea might be due to lesions of the brain stem and regions associated with the regulation of breathing. Furthermore, heart failure, metabolic and toxic encephalopathies might lead to central apnea. Central apnea might happen both in sleep and during wakefulness. *Night and morning headaches*: their relationship with sleep disturbances and neurological diseases is important. In the presence of morning headaches, one should consider problems related to sleep and respiration. This headache is diffuse and blunt in nature and is related to a decrease in O_2 saturation. Cluster headaches typically appear during REM sleep. *Cataplexy*: It is the sudden loss of muscular tonus triggered by intense emotional stimuli and physical exercise. It is described as muscular atonia or hypotonia ranging from couple of seconds to couple of minutes in duration. If this symptom is together with sleepiness during the day, then it is always related to narcolepsy. The fact that consciousness and memory are preserved during the incident differentiates cataplexy from syncope and epileptic seizures. *Sleep paralysis*: it is the carrying over of REM sleep related atonia to wakefulness. The duration of the incident is limited to seconds or minutes. When the episodes become more frequent and they last longer, this disturbs the patient significantly and even be frightening. Despite the patient is awake, visual and auditory hallucinations might be present. In order not to experience this situation during sleep, the individual avoids to sleep and develops insomnia. Narcolepsy, depression, alcohol use, sleep deprivation and shift changes are instances where this symptom might be seen. *Hypnagogic and hypnopompic hallucinations*: hallucinations taking place during the beginning of sleep are called hypnagogic, those appearing while the individual is about to wake up are called hypnopompic. These hallucinations might have visual, auditory and tactile components; they can either be pleasing or frightening. Other than being seen during narcolepsy, they can happen in instances of sleep deprivation or when there are changes in sleep patterns as well as following alcohol consumption. *Parasomnias and movement during sleep*: parasomnias are involuntary physical events that take place when an individual is about to fall asleep, during sleeping and when he/she is about to wake up. the activation of the central nervous system during parasomnias results in features caused by activation of autonomic nervous system and motor activity. NREM parasomnias are disturbances in waking up from NREM sleep and the most common are confusional arousals, sleep terror, and sleepwalking. They mainly appear during deep slow wave sleep especially during the first 1/3 of the night. Familial characteristics are prominent. Despite the patient might seem like awake during the incident, arousal is not complete and he does not interact with his surroundings, does not respond to external stimuli, is not easily arousable, resists to

efforts of waking him up and can show agitation. Patients are difficult to arouse during the event but if awaken they are confused; when episode ends, he can easily fall asleep after going to bed and does not remember the episode the next day. *Movements associated with sleep*: during REM sleep, muscle tonus disappears. REM sleep behavioral disturbance (RBD) is a parasomnia associated with REM sleep during which muscle tonus does not disappear but increases. As a result of this, the patient starts playing her/his dreams. It is characterized by aggressive behavior like speaking, shouting, kicking, punching or slapping, jumping, running which include violence and might harm the patient herself and her bed partners. The most important difference of arousal disturbances from NREM parasomnias is the development of episodes towards morning hours when REM sleep intensifies, when the patient wakes up after the episode, he is not confused and can remember a dream that can explain her/him behavior during which s/he has frequently felt threatened. Most of the patients are in the advanced age group and are idiopathic cases. Associated neurological diseases are "Parkinson's, Multisystem Atrophies and Dementia with Levy Bodies". The condition can also be seen in individuals using tricyclic antidepressants, monoamine oxidase inhibitors and serotonin reuptake inhibitors and in those who have recently stopped consuming alcohol. *Talking during sleep*: these are vocalizations ranging from murmuring to meaningful conversation during superficial NREM sleep. They can rarely be seen during REM stage as well. Stress, febrile diseases and frequent sleep deprivation can result in this. There is no need for treatment if there is not any underlying sleep disturbance. *Bruxism*: it is a movement disorder characterized by repetitive rhythmical jaw clenching and ensuing teeth grinding. It increases with stress and can result in face pain, jaw pain, teeth pain and damage to the teeth and even breaking of teeth as well as jaw dislocation. *Rhythmical movement disorder*: these are stereotypical movements that start immediately before falling asleep and continue during superficial sleep. The most known one is to rhythmically knock the head on the pillow or the headboard. It is a phenomenon usually encountered during infancy or early childhood and it disappears with increasing age by decreasing in intensity. *Restless leg syndrome (RLS) and periodical leg movements (PLM) during sleep*: RLS usually appears during evening hours and mostly after going to bed. These are unpleasant leg symptoms that cannot be well expressed by the patients. The disturbing sensation leading to an irresistible need to move the legs is the most important feature. As symptoms disappear with movement, patients constantly move their legs while in bed and they can even stand up and start walking around after a while. When patients come to see a physician with the complaint of insomnia, antidepressants that might be prescribed for treatment can increase the severity of RLS. Other causes that can increase the severity of the symptoms can be listed as: "Iron deficiency anemia, B_{12} and folate deficiencies, uremia, spinal cord lesions, diabetes mellitus, peripheral neuropathies, excessive exercise and caffeinated beverages". *Signs in children*: although they might be non-specific, the physician should definitely take sleep disturbances into consideration in children coming with the following complaints: "Developmental delay, decrease in school performance, distractibility, hyperactivity, moodiness, stubbornness and aggression". School-age children can admit to doctors with complaints of feeling themselves not rested throughout the day, not having slept enough, difficulty in concentrating, adenoid hypertrophy, lack of attention and sleepiness during classes. In the presence of such symptoms, diagnoses of sleep apnea, insomnia, RLS, hypersomnia and narcolepsy should be considered [47–54].

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