Chapter 3

Sleep and Health: Role of Dopamine

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Abstract

Introduction: Sleep is an important part of people's lives and proper sleep is a prerequisite for good health.

Purpose: The purpose of this chapter is to highlight the importance of sleep in the promotion of health, sleep-related patients, and dementia at various stages of the age of the immortal. It also refers to sleeping on Parkinson's disease and dopamine.

Material & methods: An extensive review of the relevant literature was performed via electronic databases (Medline, PubMed, Cinahl and Google Scholar) and Greek and international journals.

Results: Sleep is described as a special state of consciousness. It is composed of phases and is characterized as relatively unresponsive to the surrounding area. It is a periodic situation. The fall of consciousness during sleep provides time for the body systems to be reconstructed and renewed. Thus, sleep is a corrective mechanism that contributes to the regeneration of the person's normal and emotional state. It occurs cyclically, usually once a day. Sleep is divided into two types, known as REM (Rapid Eye Movement), and NREM (Non Rapid Eye Movement).

Conclusion: Sleep occupies about one third of our total lifetime and is a very important biological function. Its functional significance is related to the resting of brain function and to the proper functioning of memory and learning.

Keywords: sleep, health, disease, Parkinson's disease, dopamine

1. Introduction

Sleep is an important part of people's lives and proper sleep is a prerequisite for good health. People have a need for a steady sleeping period of about 7–8 hours, especially during the night [1].

The reasons that gave rise to the need for sleep and the way the sleep was incorporated into the biological cycle are one of the great mysteries of evolution. The only thing we know for sure is that our sleep is necessary in order to be able to work during the day, so its disorder in any way adversely affects our everyday lives. Physical, mental and social well-being, as well as protection from certain illnesses and accidents, depends on the quality and the quantity of sleep [2].

Sleep, therefore, is a basic necessity of the human body and at the same time a basic prerequisite of its good health, in order its normal functions to be carried out. As a result, any sleep disorder has a direct impact on the body function, reducing its performance [3].

Recognizing the significance of sleep for the human's health, the World Health Organization introduced 21st of March as World Sleep Day [4].

In this section, ancient Greeks' perceptions about sleep, its benefits and its importance to the well-being of people of all age groups as well as its importance to the patients, are mainly presented. At the same time, the measures and the ways of defending and promoting it are also highlighted.

2. Sleep concepts in antiquity

In ancient Greek Mythology, "Sleep" and "Death" are twin brothers, "wretched Gods" who lived in Tartarus, children of Night and Erebus [5].

The sleep was worshiped in the mainland of Greece. Significant centers of sleep's Worship were Epidaurus, Troizina and Olympia. He was a young man, handsome, with wings on his shoulders, who made the tired people being asleep. It was sometimes pictured as a handsome, young man who was seeding sweet dreams in the earth or he was sleeping in a bed, and some other times it was pictured as a demon with wings that was carrying a dead man to death. Indeed, it is said that he has made the leader of gods, Zeus, being asleep, despite his will, following pressure from the goddess Hera, who wanted to influence the evolution of the Trojan War [6].

One of their many children was Morpheus, the God of Dreams. He was the only god who could intervene in the dreams of kings and heroes. He was transferring gods' messages to the mortals in the form of dreams and he could take any human form himself and appear in dreams. He had the capacity to send images to people's dreams or visions, to shape them, and to form the beings that lived in them [7].

Of their other sons, Phobitoor was responsible for nightmares and he was taking animal or monster styles. Fantasos was creating surreal images by taking forms of objects such as stones or woods and Cecil was helping those dreams' aspects that portrayed reality by making dreams realistic.

God Hermes, one of the 12 Olympian Gods, was also the God of Sleep. The Romans, respectively, considered Somnus as God of Sleep [8]. The Greek philosophers expressed their views about the dreams and their interpretation in various ways. Empedocles, Plato, and Aristotle had particular approaches to the subject, based on the "clairvoyant's dreams", giving rational and not metaphysical interpretations [9].

Aristotle recognizes the preservation of living beings as the purpose of sleep claiming that all living organisms that are in move are intended to rest, fact beneficial and necessary. A living organism, according to Aristotle, cannot constantly be in action and it is not possible to have his senses in full operation incessantly. Based on this and since it is not possible for the same living being to be simultaneously in two opposite situations, the philosopher logically concludes that the animal from the situation of wakefulness passes to sleep [10].

He also determines sleep through the concept of wakefulness, posing it to the opposite function from that of sleep. These two functions take place in the same part of the body, in the place they are produced themselves. Furthermore, he believes that the way we can perceive awake man, in exactly the same way we perceive asleep one. Subsequently, he stresses the meaning of senses, always in relation to wakefulness and sleep, and states that someone who is awake, has his senses in use, as he perceives the external things and his internal movements, fact that does not happen to the person who is sleeping. Thus, he ends up linking these two passions (sleep–wakefulness) with the esthetic part of the soul, meaning the use of senses during the wakefulness period and their lack or weakness during sleep [11].

The approach of Heraclitus has contributed a lot to the sleep and dream issue. Heraclitus describes sleep as a temporary death of consciousness, where vision disappears and self-consciousness is lost. At this point dreams come about, but they do not dissolve the darkness of this conscious "Night", where the sleeping person is retreated to a place entirely subjective, in which he has no consciousness of his identity. During sleep the individual "touches" the "dead", while when he is awake, touches the man who is asleep.

Heraclelian philosophy generally rejects any idea of the objective dreaming, since it believes that the true nature of the beings is perceived exclusively by the mind [12].

Sleep was also involved with the art in many forms and often it is imprinted as eagle or butterfly's wings on the front, or with a horn from which the dreams are spreading [8]. In ancient art, sleep is portrayed as a naked young man, sometimes with beard and feathers on the head, or as an asleep on a bed of feathers with black curtains around, while Morpheus prevents any noises that could awaken him.

In the Kypselo's Ark, in Olympia, the two brothers, Sleep and Death, are depicted as little boys sleeping in their mother's arms, Death is painted in black tunic and Sleep is painted in white. In Sparta, his depiction is always accompanied by that of Death, and in the following years Death and Sleep merged into a deity [13].

2.1. Orphic hymn for the god of sleep

> *"Oh! The sleep, the king of all blessed gods and mortals, and all the animals that are fed by the broad earth, you are the only ruler of all, and come to all, and you can bind the bodies with bonds that are not made of copper.*

You release us from the cares and give us sweet relief from the labor. You make us a sacred consolation for all sorrows and you also bring us the preaching of death and you save our souls, because you are by nature the true brother of Lethe and Death. But, oh! Blessed god, please, I ask you to come together with sweetness and to save the mystics favorably for the divine works" [14].

3. Normal sleep

Sleep is described as a special state of consciousness. It is composed of phases and is characterized as relatively unresponsive to the surrounding area. It is a periodic situation. The fall of consciousness during sleep provides time for the body systems to be reconstructed and renewed. Thus, sleep is a corrective mechanism that contributes to the regeneration of the person's normal and emotional state. It occurs cyclically, usually once a day. Sleep is divided into two types, known as REM (Rapid Eye Movement), and NREM (Non Rapid Eye Movement) [15].

NEM sleep is referred to as calm sleep and its awakening becomes more difficult. It passes from four phases. In the second type, we distinguish four (4) additional phases, which follow a specific repeating pattern throughout its duration [16].

(a) ***Phase 1:*** The first phase is subjectively considered to be lighter than the others and is often seen as a transition from the state of alertness to sleep. The person wakes up much more easily, the heart and respiratory rate falls slightly. At this stage a progressive muscle relaxation takes place, the body deeply sinks into an unconsciousness stage and faint images associated with the world of dreams are apparent. Electroencephalographic waves are observed similar to those observed during wakefulness (alpha waves with a frequency of 9–12 cycles) [17].

(b) ***Phase 2:*** The second phase is characterized by light sleep. The heart and respiratory rate is decreasing, body temperature and metabolism are decreasing. The second phase lasts about 10–20 min and includes 50–55% of total sleep. The eyes begin to turn around slowly. The slightest noise can wake the sleeper. It is distinguished by an encephalogram showing the characteristic groups of cells called sleeping spindles.

(c) ***Phase 3:*** The third phase marks the onset of deep sleep. The person wakes up with difficulty and rarely moves. It takes about 15–30 min and includes 10% of our sleep time. Heart rate, blood pressure and body temperature are decreased. Beta waves (a frequency of a wave per second and five times wider than alpha waves) occur in the electroencephalogram [18].

(d) ***Phase 4:*** The fourth phase is characterized by deep sleep. The heart and respiratory rate falls to 20–30% lower than that of wakefulness. This phase lasts about 15–30 min and occupies 10% of sleep time. The person is quite loose, rarely moving and difficult to awaken. Blood pressure, heart rate and body temperature have reached the lowest values. It is said that this phase promotes the physical state of man. Delta waves appear in the encephalogram [19].

Every night, when the person is getting ready for sleep, the body temperature decreases, the breathing becomes slower, the muscles relax and the person begins to yawn. The yawning is a prolonged breath and acts as a protective device to provide the body with oxygen when a fall in breathing occurs during sleep [20].

After the pre-mentioned four phases (in the meantime, almost ninety (90) minutes have elapsed since the person fell asleep), suddenly in the encephalogram there is a completely different phase from the previous ones. Alpha waves reappear, and the brain suddenly has a great activity as if awake. Circulation and temperature are increased. Diagrams showing the activity of eye bulbs (called nystagmograms) show a significant effect. It is what is called the REM phase, the phase of traditional sleep, where dreams appear [21]. The person in this period turns to bed. During the night, each person usually dreams 90 min, divided into 5–6 phases of REM. The duration of this special phase tends to increase during the night. So the first phase, which generally appears around at midnight lasts 6–10 min, and the last, about 5 in the morning, lasts about 20 min [22].

REM sleep is referred to as paradoxical or active sleep. During it, effects from the sympathetic nervous system prevail. It is said that this type of sleep restores the individual's mental state, in particular the functions related to learning, psychological adaptation and memory. It reviews processes and events that happened during the day, as well as other accumulated information [23].

The body seems to be paralyzed while the temperature, blood flow and oxygen consumption in the brain is increased. Moreover, heart rhythm, blood pressure and heart rate are elevated, the levels of which touch those of wakefulness. The rate of breathing varies from very fast, to very slow with periods of apnea [24].

In particular, REM sleep and the 4th phase NREM are of particular interest. Selective loss of either or both types of sleep creates need for replenishment. Thus, the body the next night increases the percentage of sleep and covers the gaps. This process is called replenishment phenomenon (Rebound effect) [25].

The body function presents daily high and low periods of physical and mental activity, which is determined by the so-called biological clock or circadian rhythm. The fact that man performs his duties during the day and night is asleep, suggesting that the biological clock initially is synchronized with the natural environment [26].

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The biological rhythm of sleep is often synchronized with other body functions, such as changes in body temperature associated with sleep patterns. The maximum body temperature value occurs normally in the afternoon, decreases progressively and falls sharply as soon as the person falls asleep [32].

The typical total length of 24-hour sleeping time varies 10 times between the species from about 2 hours in the giraffe to 20 hours in the small brown bat, while in humans it lasts about 8 hours. Nighttime sleep usually occurs in humans and many other mammals, but in some mammals occurs during the light period, as in rodents [33].

All people are asleep, although everyone has different behaviors in sleep. Some people need about 7.5 hours to rest and others need less or more sleeping hours. Younger people require more sleep than older people. As long as a person stays awake, the faster he wants to fall asleep.

People are usually sleeping supine and having their eyes closed. This is not the case in some mammals that sleep with their eyes open, like the ox. Moreover, others sleep while hanging their limbs, like the bat, and others while standing, like horses [34].

The movement during sleep is relative. Some people during sleep walk or speak and the fish swim. In general, the response to endogenous and exogenous stimuli, decreases, is not removed, and this condition is reversible. Response to stimuli and reversibility are two characteristics that clearly differentiate sleep from death, coma and narcosis [35].

Sleep is also connected with a variety of physiological changes associated with breathing, heart function, muscle tone, temperature, hormone secretion and blood pressure. Data from various studies have shown that from 4 am, body temperature, blood pressure, plasma cortisol concentrations and adrenaline increase in order to prepare the individuals, when they wake up, to be ready for activity. The opposite happens as the night approaches. Plasma cortisol concentrations, mental processes and body temperature are progressively reduced to prepare the individual for sleep [36].

3.1. Utility of sleep

Sleep thus is a charging of our body's batteries so that we can cope with everyday life having new forces. The importance of sleep in maintaining our body is also confirmed by serious disturbances that are caused when we do not sleep. As regards the importance of sleep, there is no longer any doubt that proper sleep is essential to good health. Physical, mental and social well-being, as well as protection from certain illnesses and accidents, depends on the quality and quantity of sleep [37].

Night sleep should be no less than 6 hours and more than 9 hours. As for the quality of sleep, which is function of the occurrence time and the relaxing effect, it depends on the lack of noise, the appropriate temperature, light meals and physical exercise. The comfort and stability of the sleeping area, as well as the observance of regular hours, also regulates the smooth functioning of sleep. This amazing sleep function seems to fulfill two functions, neurobiological and psychological [38].

The first is associated with the excretion of waste products of metabolic processes, the possibility of curing the CNS, especially in neonates and premature, by eliminating a large number of nervous stimuli bombarding the brain every day. The second is, according to Freud, a feigned satisfaction of our desires, and allows the vengeful and destructive loads to be neutralized, allowing the processing of a particular thought with consequent better acclimatization in real life. By performing these two functions, we are able to overcome intact the stimuli that usually bombard us [36]. In addition to night sleep, human health is also affected by the habit of sleeping during the day, also known as siesta. This sleep is usually short-term, mostly common at midday hours, approximately 12 hours after the nadir of normal wakefulness [1].

Lunchtime sleep (siesta) is common in countries near the equator due to climate. It is also observed when there is a night sleep deficit, like in cultures and societies where dinner is taken late at night, night sleeping does not take place before midnight, and getting up from the bed is early in the morning. Daytime sleep is also observed in shift workers, those with

hypersomnia, and in the elderly [39]. Short sleep during the day has been associated with better health levels. However, in some people this habit may have negative effects, causing difficulties in night difficulties in night sleep and delayed alertness during afternoon awakening [21].

3.2. Factors affecting sleep

Many and various factors can affect and change the type of sleep, such as the following [40]:

(a) ***General factors:*** Various life events such as noisy entertainments, intensive exercises, examinations in school or other trials, stress or stress from pressing work, etc. are included. All the above mentioned factors can change the type of sleep quantitatively and qualitatively.

Changes in sleep can also be caused by environmental causes such as bed and sleeping changes, ventilation, lighting, or noise [33].

(b) ***Personality of the individual:*** People with chronic neurosis, depression and introversion are believed to have a characteristic type of sleep. Although the total amount of sleep is increased, these people mention that they do not feel rested. Some researchers believe that increased sleep is due to the fact that during wakefulness, psychological and emotional problems were not effectively addressed [21].

(c) ***Age:*** Infants sleep more than children and young people more than the elderly. Generally, total time is increased in childhood, decreases at young age, then, it is flattened to be stabilized at this point until the advanced age. As the age progresses the number of awakenings and the time of the proportion of time during phase, changes [41].

Age of sleep according to age									
Developmental stage	Newborn	Infant	Toddler	Preschool age	School age	Teenager	Young adults	Average age	Elderly
14–16 hours/day	14–16 hours/day	12–14 hours/day	11–12 hours/day	11 hours/day	10 hours /day	7–8 hours/day	7–8 hours/day	7 hours /day	6 hours/day

(d) ***Underlying disease:*** In a large number of diseases it is possible to observe changes in the type and amount of sleep. For example, conditions characterized by pain affect the person's mood for sleeping. Nocturia, a common symptom for the elderly, can change the type of sleep. But also arterial hypertension often causes morning awakening, accompanied by a feeling of fatigue [24].

The symptoms of people with duo dental ulcer are exacerbated due to increased gastric secretions during sleep. A large number of respiratory illnesses are also involved with sleep. Additionally, the intake of certain substances can alter the behavior of sleep. L-Tryptophan is a very basic amino acid which is found in a wide variety of foods. It is believed that it reduces the onset of sleep time. Due to this property, it was considered a natural hypnotic. Moreover, man's habit of drinking a glass of warm milk before bedtime has a scientific basis, because milk contains this amino acid [42].

(e) ***Medicines*****:** The effects and side effects of medications bring about changes in sleep. Indicatively, antihypertensive and diuretics are mentioned. The side effects of administering antihistamines and antihypertensive drugs are drowsiness, night-time awakening and gait. Their beneficial effect compensates for the side effects, which can be reduced either by developing tolerance or by choosing antihistamine that has fewer side effects than the reported ones [43].

Sedatives, antidepressants and barbiturates also suppress sleep and their effects on sleep are quite similar to those observed in alcohol. From both causes, the latency of sleep time is reduced, continuous sleep and total sleep time increases and during acute drug administration, mild suppression of REM sleep appears. Very few of them promote sleep and this happens for a very short time [44].

Changes in sleep may be caused by many drug and substance groups, such as alcohol, anticholinergics, anticonvulsants, antidepressants, antihistamines, opiates, stimulants or irritants, and opioids.

Antidepressant drugs may change the type of sleep indirectly due to underlying depression, which causes sleeping abnormalities and directly due to the drug effect on sleep. The most persistent effects of antidepressant drugs on sleep are the general suppression of REM sleep and the prolonged latency of REM sleep. Sudden discontinuation of antidepressant drugs can lead to a prolonged period of REM sleep replacement, and the person usually complains about tension, dread and reduction of sleep quality [45].

(f) ***Irritants:*** Substances like caffeine or nicotine are included and they can disturb sleep. A cup of coffee, chocolate or Coca-Cola keep the person awake for several hours due to caffeine. Nicotine is considered a milder irritant but heavy smokers may experience changes in sleep. All irritants increase latent sleep time. Continuous administration, as well as immediate discontinuation has a serious effect on sleep [45].

(g) ***Alcohol***: Alcohol in a small amount promotes sleep because it causes relaxation, and in large amounts inhibits sleep. The use of alcohol leads to increased snoring and aggravates sleep apnea. With the use of alcohol may appear sleepwalking, nocturnal enuresis and in many cases nightmares. When chronic alcoholics decide to abstain from alcohol, they often experience insomnia. Alcohol withdrawal time is characterized by a decrease in overall and continued sleep [46].

(h) ***Psychological stress*****:** People who face serious personal or other problems usually develop stress that increases the tension and inhibits sleep. Continuous stress helps in getting poor sleep habits such as excessive sleep and insomnia [47].

(i) ***Exercise and fatigue*****:** Moderate fatigue resulting from exercise or from a pleasant job usually ensures restful sleep. Conversely, excessive fatigue from debilitating or stressful work can cause sleeping difficulties [48].

3.3. Sleep deprivation

Well-documented studies report that after 10 or 20 hours of insomnia, signs of excessive fatigue, reddening of the eyes, some mistakes in perception are beginning to appear. We have

the illusion that the floor waves. There is a substance in the blood, the in dole, which belongs to the same family as the hallucinogen L.S.D. [49].

If an individual stays sleepless for 60 hours, he will experience symptoms such as reduction of neck reflex, hand tremor, nystagmus, clumsy movements, eyelid dropping, dysarthria, difficulty in concentrating, reduced facial movements, and his general appearance seems to be apathetic. The changes start on the third day with illusions and as the sleep deprivation continues, perceptual, cognitive and psychomotor capacity of the individual are reduced, while visual hallucinations appear [50].

After 90 hours of insomnia, we have the impression that our face is full of spiders and it is impossible to distinguish between dream and reality. The electroencephalogram reveals the presence of a "short-sighted" period, where the person, although awake, has the same cerebrovascular features of sleep (slow waves). An individual under these conditions becomes a real public danger and can respond with reactions totally disproportionate to insignificant things [51].

Recovery from sleep deprivation is accompanied by increased overall sleep time. The values of the amount and type of the different sleep phases are restored during the first night of recovery [24].

4. Sleep disorders

Sleep disorders affect not only sleep but also many more aspects of life. They are related to adverse effects on the quality of life and health status during the day. There are three (3) main types of sleep disorders related to the biological sleep clock [28]:

(a) ***Type of delay of the sleep phase*****:** The person cannot move the time of sleep and wakes up earlier than usual, so he sleeps and wakes up slowly in relation to the existed social requirements. People with delayed sleep phase often report that they feel sleepy in the early hours but are more energetic and alert late in the evening [2, 28].

(b) ***Jet lag type*****:** The cycle of sleep and activity for most people is synchronized with the pace of day and night at the geographical point where they live and work. Jet lag is due to the de-synchronization between the various rhythms of the organism and the environmental rhythms. The rhythm that is most affected is the cycle of sleep and activity, with the associated changes in physical and mental functions. Symptoms of this syndrome are somnolence, fatigue, difficulty of concentrating, and irritation during the day. People, despite their fatigue throughout the day, cannot sleep and their sleep is anxious. This syndrome resolves in 2–7 days, depending on the travel distance from east to west and temperamental sensitivity [21].

Many people think they can avoid symptoms by changing eating and sleeping times before traveling. Others also think that the onset of the syndrome is directly related to lack of sleep, so sleep is the solution itself. Special treatment is not required [29].

(c) ***Type of shift change*****:** This disorder is due to people working on night shifts or frequent shift changes. Shifts disrupt the worker's biological rhythm. Rolling working time creates short- and long-term health effects. Effects include sleep disorders, cardiovascular

disease, gastrointestinal disturbances and aggravation of chronic conditions. Young people and teenagers tolerate rolling schedule, showing fewer symptoms than the elderly [30]. It accounts for 10% of shift workers, which necessarily include night shifts. People's sensitivity to program changes varies widely, and a respected number of people simply do not adapt to changing hours. These people should not be employed on such a timetable. In this case, things are therapeutically more complex, because it is not always easy to change the individual's job. This is a medication that induces vigilance 30–60 min before the job, which is combined with the treatment of insomnia that occurs when the person wishes to sleep during the day [31].

4.1. Effects of sleep disorders

Sleep disorders can have serious effects on memory, learning, cardiovascular, nervous system, reduced productivity, our social behavior, and general deterioration in quality of life [52].

(a) ***Physical effects:*** Inadequate sleep has a serious effect on physical health resulting in illnesses such as diabetes mellitus, hypertension, heart disease, osteoporosis, various inflammations and many forms of cancer, especially breast and colon cancer [53]. These health problems arise from the production by the body of stress-related hormones, causing hypertension, which in turn is one of the main causes of heart attacks. Inadequate sleep increases blood levels of interleukin, resulting in increased fever, fatigue and loss of appetite. People suffering from insomnia produce elevated levels of cortisol, which is directly related to health problems as already mentioned [54].

(b) ***Psychological effects:*** Sleep and mental mood are characterized by a two-way relationship. As long as sleep affects mental mood, equally mood affects sleep. The lack of sufficient or good sleep adversely affects mental health, resulting in mental disorders such as depression, anxiety, alcoholism [33].

(c) ***Social-economic effects:*** Sleep disorders are associated with a negative impact on social behavior related to deterioration in quality of life, reduced productivity, excessive use of health resources, etc. Furthermore, there are direct adverse economic consequences due to medical costs, medications, medical consultations, examinations, investigations and inpatient and out-patient hospitalization. Indirect consequences are also apparent due to absences from work and the overall efficiency of the individual throughout the day [55].

4.2. Sleep and diseases

To a large number of diseases, changes in the type and amount of sleep may occur. For example, conditions characterized by pain affect the person's mood for sleeping [56].

4.2.1. Sleep in Parkinson's disease

Parkinson's disease is an age-related disorder characterized by movement disorders such as stiffness of the body, slowing of movement, and trembling of limbs when they are not in use. In advanced stages it progresses to dementia and eventually death [57]. The main symptoms are caused by the loss of dopamine-secreting cells in the substantia nigra [58].

More than 96% of patients suffering from Parkinson will experience sleep disturbances during the course of the disease. They are due to the interaction of various factors, such as motor problems (stiffness), circadian rhythm changes in sleep–wake cycle, behavioral disorders in sleep REM, psychiatric problems (anxiety, depression, dementia), side effects of drugs. It should be noted that the treatment of Parkinson's disease among its side effects includes sleep disorders characterized by daytime sleepiness [59].

Apart from the breakdown of nighttime sleep of the reported causes, 15% of patients with Parkinson will develop sleepiness throughout the day during the course of the disease. It is a sudden advent of sleep, in an inappropriate environment, without warning and without the possibility of suspension. Daytime sleepiness may be due either to the progression of the disease or to the various disorders that interrupt nighttime sleep or to the side effects of anti-Parkinsonian drugs [60].

Regarding the treatment of sleep disorders in Parkinson's disease, it aims to treat each individual disorder separately. In each case it is personalized. The basic principle of treatment is not to use plethora of sedative and hypnotic drugs. The medication is aimed at regulating anti-Parkinsonian treatment to reduce the kinetic problems that disturb sleep [61].

Dopamine is an organic chemical that plays several important roles in the brain and body. Also it is an amine synthesized which is synthesized in the brain and kidneys. Therefore in the brain, dopamine functions as a neurotransmitter and send signals to other nerve cells. The brain includes several distinct dopamine pathways, one of them plays a major role in the motivational component of reward-motivated behavior [62, 63].

In particular, dopamine is an organic substance used by nerve cells to communicate with each other. Dopamine acts on receptors found in the immune system cells and all dopamine receptor subtypes are found in lymphocytes. Several diseases have been found to be associated with damage to dopamine system. Dopamine deficiency caused by Parkinson's disease is associated with reduced movement, fatigue, slowing or blurring of cognitive functions, stiffness, loss of initiative or mobilization, and aggressive behavior in competitive situations [64].

Dopamine is available as an intravenous drug that acts on the sympathetic nervous system, with an increase in heart rate and blood pressure. However, due to the fact that dopamine cannot cross the blood–brain barrier, dopamine given as a drug does not directly affect the central nervous system. To increase the amount of dopamine in the brain of patients with conditions such as Parkinson's disease and dystonia, L-DOPA (which is the dopamine precursor) is often prescribed, because it crosses the blood–brain barrier [65]. Although L-DOPA treatment cannot restore the dopamine cells that have been lost, but it causes the remaining cells to produce more dopamine, thereby compensating for the loss to at least some degree [66].

Some medications act as dopamine agonists and can treat its low levels (hypodopaminergic) as they are typically used to treat PD, attention deficit disorder, hyperactivity disorder, certain mucosal tumors (prolactinoma), and they can also be useful to restless legs syndrome (RLS) [61]. For the treatment of Parkinsonism drugs such as bromocriptine and pergolide are sometimes used, but in most cases L-DOPA appears to give the best trade-off between positive effects and negative side-effects [66]. The development of a dopamine dysregulation

syndrome is sometimes associated with dopaminergic medications, which involves the overuse of dopaminergic medication and medication-induced compulsive engagement in natural rewards like gambling and sexual activity [67].

Restless legs syndrome (RLS) is a common sensory-kinetic disorder characterized by abnormal sensations that appear initially at rest or during sleep, relieved by the movement of the affected limb. The pathophysiology of RLS remains unclear although the role of dopamine dysfunction and iron deficiency in the brain, have been suggested [68].

Symptoms include unpleasant sensations in the extremities, especially in tibia. They can appear on both legs, sometimes also offend the hands. Individuals who have the syndrome usually report symptoms described as chills, tingling, burning, pain, pulling or even as something creeping under the skin. Symptoms get worse when the patient rests and they are improved with the movement. Symptoms are usually getting worse in the evening and during the night, so these patients often have poor sleep quality and consequently often experience daytime sleepiness. It is noted that there is no cure for this syndrome [65].

Treatment with dopaminergic agonists relieves symptoms, but does not result in total healing [69]. Adherence to the hygiene rules of sleep is also important. At the same time, psychiatric help is sought if the disorder is due to a psychiatric problem [56].

It is also noted that Researchers from the University of Barcelona and the Centro de Investigacion Biomedica en Red de Enfermedades Neurodegenerativas (CIBERNED) in Spain has discovered a new function of the neurotransmitter dopamine in controlling sleep regulation. The act of Dopamine in the pineal gland is central to dictating the 'circadian rhythm' in humans -- the series of biological processes that enables brain activity to adapt to the time of the day [70]. The translation of the light signals from the pineal gland which is received by the retina into a language understandable to the rest of the body [71]. In conclusion, the formation of these heteromers is an effective mechanism to stop melatonin production when the day begins and to 'wake up' the brain. This new function of dopamine could be extremely useful when designing new treatments to help mitigate circadian rhythm disturbances, for example those related to jet lag, those found among people who work at night, and in cases of sleep disorders in general [72].

4.3. Obstructive sleep apnea and diabetes mellitus

Most patients with diabetes mellitus (SC) have insufficient sleep in duration and quality. On the other hand, short-term and poor-quality sleep seems to adversely affect glucose metabolism and is associated with an increased risk of developing AD1 [73].

Patients with diabetes mellitus (SC) suffer from obstructive sleep apnea very often. It is likely that AD increases the risk for development of obstructive sleep apnea, mainly through the mechanisms of inflammation and autonomic nervous system (ADN) dysfunction. Additionally, diabetic neuropathy is associated with increased sensibility of promectal chemoreceptors to CO2, and sensitivity of peripheral chemoreceptors decreases [74].

Obstructive sleep apnea syndrome (OSAS) is a disorder that is characterized by repetitive partial or complete closure of upper airway during sleep. Also, obesity is the most important risk factor for OSAS. Many case studies in the literature show that OSAS is associated with insulin resistance, glucose intolerance and type 2 diabetes, independently of shared risk factors [75].

4.4. Sleep in chronic kidney failure

Sleep disturbances are very common in patients with chronic kidney deficiency. Pathophysiology is complicated and may include a combination of factors such as fluid balance, anemia, cardiovascular function, concomitant diseases, medications, physique, psychosocial and demographic factors and everyday habits. Recognition and treatment of these disorders can improve the quality of life and reduce morbidity and mortality in this patient [76].

The most commonly reported complaints are insomnia, Restless Legs Syndrome, sleep apnea and excessive daytime sleepiness [77]:

(a) ***Insomnia:*** Insomnia is common in CKD patients. There is a reduction in total sleep time of 4.4–6 hours and fragmentation due to a high percentage of microalarms - awakenings resulting in sleep efficiency ranging from 66 to 85% [49].

(b) ***Drowsiness:*** Daily drowsiness is common in patients with chronic obstructive pulmonary disease and correlates with uremic levels and periodic limb syndrome.

(c) ***Sleep impaired sleep syndrome (SASY):*** The most common symptoms of SASY is daytime fatigue, depression, cognitive impairment, which can be mistakenly attributed to Chronic Kidney Deficiency or other similar situations, and thus to undergo a subdiagnosis of SASY in these patients [55].

(d) ***Restless legs/periodic movement syndrome (sleep apnea):*** A rate of up to 80% of patients with restless legs syndrome (sleep deprivation syndrome) has an increased number of stereotyped movements of the legs called periodic movement of the tip (PKA). These increased and often intense movements of the limbs can last from a few minutes to a few hours. As a result of this, the patient experiences a lot of wakes and awakenings which in turn disrupt the normal and sleeping function of the sufferer [78].

5. Sleep and age

Age plays an important role in sleep duration as well as the formation of its internal architecture. As a person grows up, average sleep time falls from 16 to 18 hours for infants to 8 hours for a 12-year old child, then 7.5 hours for people between 25 and 45 and 6.5 hours for the elderly. Alongside with age, two things increase: the latent time that sleep comes and alertness time after sleep begins, that is more awakenings and inability to sleep again take place [39].

5.1. Sleep during infancy

During the first weeks of the infant's life, awakening at regular times during day and night is considered completely normal. Infants usually sleep all day with few intervals. The sleep-awakening cycle includes sleep and waking up for feeding and diaper change. Infants usually have an irregular such cycle and sleep 10–18 hours a day [79]. In order to develop the right models of sleep, babies have to go to bed when they feel sleepy and not when they are already asleep. Moreover, they have to learn to sleep by themselves from their first months. At the same time exposure to the sun and playing under it can guarantee a quieter sleep at night.

A baby's sleep gets more normal from the 4th to the 6th month because later it gets more difficult. Sleep duration is determined by neurological maturation, temperament factors and the baby's emotional state. When the baby has a troubled sleep, a sleep steady schedule needs to be followed [80].

The infant needs to sleep in specific hours during day and night, in a specific environment and with the following characteristics [38]:

- In its cot or basket with a stable and not very soft mattress.
- Low lighting.
- Noise-free.
- With relaxing music over its bed.
- With one of the baby's favorite dollies.

In the first 3–6 months, even if the baby has its own room, it is more practical for the cot to be in the parents' bedroom, so that they can feed it as easily as possible. Room temperature needs to be between 18 and 22–23°C. Its pajamas have to be light, the bed linen to be a light feather or woolen duvet or sleeping bag in winter, and in summer a sheet or cotton blanket is enough [81].

If the baby finds it difficult to sleep at night then a series of specific actions before sleep take place, such as a bath, a tender hug, lullaby or kiss, so that the baby can connect sleep to a pleasant feeling and sleep faster.

When it wakes up and cries at night make sure to see if it is hungry or its diaper wet, so as to give it milk or change the diaper. If it is in colic pain, rub its belly with oil. When the first teeth start to grow, you can put some gel on its gums to relieve pain after consulting the doctor [38].

For infants up to 1 year old the 'sudden infant death syndrome' is the first cause of death. Diagnosis takes place after ruling out all other possible causes of death. Breathing or heartbeat problems during sleep could be partially the cause as well. Death comes after arterial pressure falls and heartbeat slows down gradually till it stops. Main risk factors include smoking or drug use by the mother during pregnancy and after labor, cold winter weather and a baby's face-down position during sleep [82].

5.2. Sleep in children

Children's sleep changes with age. Before the 3rd month of life they pass from alertness to sleep with REM sleep directly, whereas after their 3rd month with NREM, like adults. The REM sleep rate changes as well. For a newborn it is 50%, while gradually it falls to 20–25% until the child is 3 years old [65]. Normal sleep duration also changes with age. For newborns it is 16–18 hours, for infants 13–15, preschool age 12–13, school 11–12 and in adolescence 9 hours. Usual sleep start time in toddlers is 8–8:30 p.m., while for teenagers it is 11–11:30 [81].

Sleep is a vital part of children's healthy development and is related to their physical, cognitive, emotional and social growth. In most cases sleep disorders are temporary, without long-term results. For some children, however, they can be very important [36].

In children sleepiness due to lack of sleep manifests as lack of attention, hyperactivity or aggressiveness. Lack of attention then has consequences on memory and learning. Quite often parents do not mention their child's sleep problem to the pediatrician or do not see the relation between sleep disorders and behavior during daytime. Thus, in a routine visit to the doctor questions about sleep need to be asked [83].

In pre-school children parasomnias are common, for instance nightmares, talking through sleep or night terror. Their frequency gradually decreases during the first 10 years of life. Most common sleep disorders in children are [81].

5.2.1. Behavioristic insomnia

Two types of it are often present in the same child. In the first, the child resists verbally or postpones sleep claiming fear, or leaves the bed and goes to find the parents. If time is lost its sleep is inadequate. The second type is about continuous night awakenings. The child that is used to going to bed under certain circumstances, like feeding or rocking in parents' arms, cannot calm down if it wakes up and cannot go back to sleep without the parents there [38].

Treating behavioristic insomnia: If all other medical problems are ruled out, like belly pain, breathlessness, otitis, allergic rhinitis, atopic dermatitis, underlying neurological disease or pharmaceutical effect, then the following measures are taken [84]:

- Steady sleep routine, around the time pre-school children go to bed (around 8–8:30). This should start 20–45 min before desired sleeping and include a bath, clothes changing, story narration or a game or blanket.
- The child should be in bed before falling asleep and not after.
- For children who wake up at night 'systematic indifference' is followed, that is no help is given to sleep again at night, so as to eliminate the need for a parent to be present (graduated extinction).
- The parent leaves child's room before it falls asleep. Every time it wakes up and looks for them, they have to wait more and more before answering.
- A positive behavior needs to be strengthened through reward.

Research shows that interventions in behavior clinically improve 80% of children to a great degree. No child showed any side effects from these treatments, and there is also a great secondary benefit in improving the daily behavior, self-confidence and mental health of the child and the parents [85].

5.2.2. Parasomnias

These are undesirable natural events or experiences that occur during sleep, during sleep or awakening. They are considered benign phenomenon in children and – if not very common and intense – they do not affect the duration and quality of sleep. They may exist individually in a child or co-exist with neurological psychiatric or other problems. Often there is a similar background to one of the parents [79].

The most common parasomnias in pre-school children are [81]:

- *Conjunctive awakening*. It occurs in children less than 5 years of age, 2–3 hours after the onset of sleep (NREM sleep disorder). The child sits on the bed restless and crying, or grumbles, can say something like "go" or "no" and does not calm down with what the parents say. The episode lasts 10–30 min and then comes back. Confusing awakens do not show stereotypical motions, sweating or flushing [81].
- *Nightmare*. The typical age for night terrors is 4–12 years old. The child wakes up with intense crying, has the same behavior as confusing awakening, with the difference of the presence of disturbances from the autonomic nervous system, that is, it is sweaty, has tachycardia and flushing. He does not seem to listen to the parents, he can jump out of bed as if he wants to avoid a threat, and in the morning he does not remember the episode [86].
- *Sleepwalking*. It is a NREM sleep disorder, which is most often seen in children aged 8–12, and this is because many episodes occur in infancy (e.g. the child is getting up and going to find his or her parents, or just going around In his cradle) go unnoticed. In sleepwalking, the child gets up from the bed and walks through the house, may seem uncomfortable and run around, or do simple activities that seem to be deliberate, like going to the bathroom. Especially for *sleepwalking,* where there is a risk of injury, preventative security measures such as locking the front door, guard rails on the ladder, removal of sharp and fragile objects, as well as floor barriers, a low bed, etc. should be taken [87].
- *Talking through sleep*. This is not pathological. It is the most common of all disorders [81].
- *Tooth grinding*. Also a frequent disorder in which the child sheds or tightens his teeth to sleep. When it is systematic, there is risk of tooth decay [88].
- *Nightmares*. It is a disorder of REM sleep and occurs more often in the early morning hours when it is more abundant. These are unpleasant, disturbing or even disgusting dreams that awake the child. When he wakes up, he is fully alert and older children remember to describe what happened. It is short-lived and the child continues to sleep. Children with post-traumatic anxiety disorder have more nightmares [89].
- *Night urination*. These are episodes of urinary incontinence in sleep, which occur at least twice weekly in children over 5 years of age. The majority of children gain control of the bladder until this age. These episodes can occur in all stages of sleep. They are either primary, when there has never been a period without enuresis, or secondary, which recurs after a period of at least 6 months and in this case may be associated with infection, diabetes, sleep apnea or other disorders [86].

Treating parasomnias: It is usually enough for the parents to reassure the child or stay with him until the end of the episode, while using various behavioral techniques such as programmed awakening. Drug administration is limited to selected cases of very resistant forms or to children with severe neurodevelopment problems and is given for a short time [81].

5.2.3. Respiratory disorders in sleep

It is a range of disorders ranging from simple snoring to classic obstructive sleep apnea, sleep apnea, or central hyponatremia syndromes [82].

Moreover, 10–12% of children snore, but even this disorder, which is otherwise benign, may have neuropsychiatric effects such as more anxiety, attention deficit disorder, social problems and depression. The most frequent and most important of all respiratory disturbances of sleep is obstructive apnea. These are episodes of partial or complete obstruction at the air intake during sleep, resulting in a reduction in oxygen in the blood [90].

The most common causes are hypertrophic tonsils and adenoids (carnations), craniofacial abnormalities, obesity and neuromuscular diseases. These recurrent sleep obstructions often result in waking up and a decrease in deep and relaxing sleep. The child can snore, sleep with open mouth, and wake up often to get breath, sound like drowning, getting night terrors or enuresis, sleepwalk. During the day it presents drowsiness, distraction, reduced academic performance, hyperactivity, and over time may present hypertension [2, 90]. Depending on the underlying cause, obstructive sleep apnea is treated with weight loss, medication, surgery, even with sleeping apnea (CPAP) devices [87].

There is also a minority of cases that need to be investigated, such as when the child snores or has sleep apnea, presents secondary enuresis, and finally to exclude *epilepsy*. Seizures, especially nighttime spasms originating from the frontal lobe of the brain, may be misdiagnosed as parasomnias [81]. Particular features from the child's history may help to distinguish. Convulsions occur at any time of the night, are stereotyped, shorter or occur several times the same night. When it is difficult to distinguish, further investigation by electroencephalography and polyp's graphic study is recommended [87].

Moreover, *narcolepsy*, although considered unusual in children, is rather sub-diagnosed. It is a disorder characterized by chronic daytime sleepiness with sleeps episodes during the day (usually 3–5 episodes lasting 10–20 min) that occur more frequently during monotonous activity. Many adult patients with postnatal narcolepsy report having symptoms as children. Narcolepsy has a genetic basis, is a chronic disease and its treatment is only symptomatic [91].

Restless legs syndrome also in some children may be synonymous with "growth pains." It is a hereditary disorder, usually a family history. This is a kinetic sleep disorder, in which the person complains about a strange, disturbing, creepy sensation on his feet, like something is crawling, appearing in the evening and at night. Some patients experience improvement by iron administration. This annoyance is temporarily relieved by the movement of the legs and so the person feels the need to shake his legs. This movement prevents him from falling asleep or breaking his sleep, resulting in fatigue and drowsiness in a day [92].

Sleep disturbances have a significant impact on the quality of life of the child and the family and are often treated easily. This underlines the need for proper diagnosis. Parents should monitor the sleeping of their children and when they recognize an unusual sleep behavior need to consult their pediatrician [81].

5.3. Sleep in the old age

When talking about sleep disorders in the elderly, we mean those that affect the ability to initiate and maintain sleep, including excessive sleep duration.

The timing and amount of sleep change with age. Elderly people tend to sleep early, wake up earlier and tolerate less changes in the sleep–wake cycle. As the circadian rhythm varies with

age, fatigue tends to become more intense as the sleep time increases. When this happens, the person wakes up earlier and the cycle repeats itself. Sleep efficiency / sleep duration compared to bedtime, decreases from 95% during puberty to less than <75% during third age [24].

Restless sleep in the elderly is due to various factors. First of all, poor sleep hygiene habits. Also, a medical or mood disorder that is adversely affected by sleep is more likely to occur, and medications to treat them may cause sleep disturbances. In addition, the possibility of primary sleep disorders, such as sleep apnea that may aggravate disturbed sleep, is increasing. Finally, aging affects the functioning of the urinary bladder, circadian rhythm, or hormone secretion and body temperature. These factors may result in less rejuvenating and more disturbed sleep [21, 93].

There are some age-related changes in sleep, although sleep disorders in the elderly may be related to psychological stress and stimuli, such as:

(a) ***Insomnia:*** It is the difficulty in the occurrence and maintenance of sleep. It may be transient (a few days), short (1–3 weeks) and chronic (>3–4 weeks). Treatment of insomnia usually does not require immediate medication. If it is nevertheless necessary on the basis of an individualized assessment, the lowest effective dose of the safest medicinal product should be used. The causes of insomnia include any medical condition, many medications and psychiatric disorders such as anxiety, dementia, and depression [27].

(b) ***Sleepiness:*** In the elderly the drowsiness during the day is persistent, excessive and does not diminish with extra sleep. It may be due to a wide variety of possible causes such as hypoglycemia, hypothyroidism, aphthous hyperthyroidism, uremia, hepatic failure, hypercapnia, hydrocephalus, head trauma, increased intracranial pressure of any etiology, etc. [26].

(c) ***Parasomnias:*** These are movements and behaviors that occur during sleep. The parasomnias that may occur in the elderly include the restless legs syndrome and periodic movements of the limbs in sleep [21].

(d) ***Sleep apnea:*** It is the temporary interruption of breathing during sleep due to airway obstruction. To combat the above sleep disorders in the elderly, it is advisable to avoid drinking before bedtime, frequent change of the diaper for incontinence, and discussing the problem with the attendant attending the elderly person with sleeping problems [3].

6. Sleep in the hospital

Sleep of the patient is a vital need and its fulfillment is a nursing responsibility. Only addressing the sleep problem requires not only specific scientific knowledge, as was said at the outset, but also a combination of nursing procedures in the context of integrated nursing care. Often, the patient does not have enough sleep, and this has an unpleasant effect on his psychosomatic well-being and resistance to the disease, as well as on health rehabilitation. In general, deprivation of sleep to a serious degree may cause disorder of thought and behavior, melancholy [21, 94].

Preparing the patients for sleeping, ensuring adequate sleep and monitoring their condition at night are unique nursing responsibilities, as no other health care profession has this concern [95]. For effective nursing care of sleeping patients, nurses need specialized knowledge from many sciences, including [21]:

- The physiology of sleep.
- Sleep disturbances and pathology.
- The psychology of sleep.
- Pain and anxiety as causes of insomnia.
- The pharmacology of hypnotics.
- The theory of dreams.
- The nursing system, such as patient preparation for sleep, night care, etc.
- The art of communication, because with this the nurse will identify and solve the problems of the patient's sleep.
- Technical nursing measures to ensure physical comfort.

As the most common causes of insomnia in the hospital environment are considered [93]:

1.	Environmentally	• Noise • Temperature • Lighting
2.	Physically	• Pain • Discomfort • Thirst • Hunger • A full bladder
3.	Psychological	• Anxiety • Overstress • Melancholy • Anger

Surveys have also shown that the factors that disturb the sleep of patients include the following [21]:

- Noise created by staff e.g. Conversations, book browses, and more.
- Noise and other environmental disturbances e.g. Squeaking doors and wheeled vehicles, sudden strikes of objects, cardio scopes, rewinders, suction fans, sliding furniture, telephones, intense lighting etc.
- Nursing and treatment procedures e.g. taking vital signs, injections, individual care.

- Noises generated by other patients, such as conversation, coughing, vomiting, snoring.
- The pathological condition of illness, pain, fever, discomfort, bedtime, lack of private space, difficulty in oral communication such as endotracheal intubation or aphasia, fear of death, and so on.

The patient struggling to sleep in so many noises reaches the point of wondering whether sleep is permitted in the hospital. Nurses again, as a health care professional, with their own personal interest, "good art" and their scientific education, have to care for the patient's exercise, keeping them busy, rest and sleep; this must be the link, the true dimension of hospitalization [94].

More importantly, nurses' responsibility in terms of sleep advancement is to help the person at all stages of the disease to ensure adequate, calm and effective sleep [93].

Information about the sleep environment is whether the person sleeps alone or shares the room with another, the number of pillows and bedding him uses ventilation, lighting and noise. Also noted are the drugs and the type they use, if they are eating before bedtime, the type of food and drink they are used to, whether they are showering or bathing before eating. In particular, the person's views on rest and sleep time he considers necessary to operate at desired levels are considered [87].

- General nursing interventions [95]
  - Help the person recognize that he is exercising control over his type of sleep, and that he can achieve restful sleep by natural means such as noise avoidance, normal temperature, and reduced light.
  - Help identify the type of sleep, sleeping habits and pre-sleep habits.
  - Help distinguish or establish a type of sleep relaxing and comfortable for oneself.
  - Encourage patient to identify the factors that affect his sleep pattern.
  - Take leisure and activity types throughout the day, in the afternoon and in the evening when planning your nighttime sleep.
- Nursing interventions for daily program [69]
  - Encourage the person to actively participate in activities appropriate to his/her situation. Design rest periods and activity for the whole day.
  - Help patients detect the time of daytime sleep. When the sleep of the day is taken at the same time and for a planned duration it is beneficial.
  - Help to avoid frequent insomnia throughout the day. Serious sufferers and those undergoing surgery will have a greater number of short-term sleep during the day.
- Nursing night program interventions [94]
  - Help the person reduce their activities before bedtime.
  - Encourage you to define and perform your pre-sleep habits and help them adapt to the hospital environment.
  - Give a gentle rub, place a suitable bed, keep it dry and clean.

- Offer them the right reading or music.
- Know that stress is more common at night. Give opportunities to the sick person to talk to you about his interests and his fears. Suggest that he discuss it with a family member or a trusted friend of his.
- Include the painkiller in the patient's program and administer it before bedtime. Although these drugs may affect the type of sleep, relief from pain is of greater importance.
- Plan hospitalizations so as not to disturb sleep, such as avoiding diuretic or stimulant administration before bedtime.

7. Conclusions

Sleep occupies about one third of our total lifetime and is a very important biological function. Its functional significance is related to the resting of brain function and to the proper functioning of memory and learning. Sleep deprivation causes disturbance of attention, performance at work and emotion.

Therefore, sleep is essential for a smooth living. Its duration is satisfactory when we wake up rested and rejuvenated. The duration of sleep differs from person to person but is estimated at about 8 hours a day. With aging, it usually reduces its duration and many elderly people sleep 5–6 hours a day.

In order to have a normal sleep, it is good to respect our biological clock that is to try to sleep for about the same hour at night and to wake up at about the same time in the morning.

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