Sleep mechanism and primary function

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Abstract

Why we sleep (1)? There is no clear answer to this Question. By the way we can look at this question from another perspective: why do we wake up and maintain wakefulness for a long time? We need wakefulness to obtain food and water, avoid danger, reproduction and lot of vital and social needing. Sleep is opposite towards of wakefulness. Sleep is a complex process and all the functions have not been clear yet (probably that' why it is named as mysteries of biology (2). Although it is necessary for human brain and body activities. Also, it has a main role in protection and survival.

Many researchers showed that the prolonged wakefulness and lack of adequate sleep lead to many diseases such as Diabetes, Obesity and Cardiovascular disease (3). Sleep plays an important role to form a new pathway and processing information in the memory, clear out toxins from brain, promote growth, support immune system, regulation many hormones which finally helps to maintain homeostasis. Sleep time is varying in people and it depends on Genetics, environment and lifestyle, but each sleep cycle includes 90-110 minutes and the number of cycles is different among people. Sleep has two parts: NREM (non-rapid eye movement or Slow waves sleep) and REM (rapid eye movement or Fast waves, or paradoxical sleep) (4).

The first one has 4 stages and during NREM the coordination between neurons become much stronger, while body activities, blood pressure and heart beats are decreased and in this stage if we saw dreams we cannot remember them, while REM sleep, that by electroencephalographic records looks like wakefulness (that's why known as paradoxical sleep (5) characterized by increasing of heart and breathing rate, is rich of emotionally colored and memorizing dreams, inhibition of the spinal cord motor neurons.

ძილის მექანიზმები და ძირითადი ფუნქციები

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რატომ გვძინავს? (1) შეკითხვაზე საბოლოო პასუხი ჯერ კიდევ არ არსებობს. მაგრამ შესაძლოა შეკითხვის მეორე ალტერნატივაც არსებობდეს - რატომ ვიღვიძებთ და ხანგრძლივი დროის განმავლობაში რისთვის ვინარჩუნებთ ღვიძილს? ცოცხალი ორგანიზმებისათვის აუცილებელია საკვები, წყალი (ხშირ შემთხვევაში მათი მოპოვება), კვება, საფრთხისგან თავის დაცვა, გამრავლება და მრავალი სხვა სასიცოცხლო, თუ სოციალური საჭიროება. ეს ყველაფერი ღვიძილის მდგომარეობას უკავშირდება. ღვიძილის საპირისპირო ძილის მდგომარეობაა. ის რთული ფიზიოლოგიური პროცესების ერთობლიობაა და მისი ფუნქციები ჯერ კიდევ საბოლოოდ დადგენილი არ არის. ძილს სხვანაირად ბიოლოგიის საიდუმლოსაც უწოდებენ (2) . ამავე დროს მისი ნორმალური მიმდინარეობა აუცილებელია თავის ტვინისა და მთელი ორგანიზმის აქტივობებისათვის და გადარჩენისთვისაც. მრავალ სამეცნიერო ნაშრომში ნაჩვენებია, რომ გახანგრძლივებულმა ღვიძილმა და ხანმოკლე ძილმა (≤ 6სთ) შესაძლოა მრავალი სომატური დაავადება - დიაბეტი, ჭარბწონიანობა, გულ-სისხლძარღვთა დაავადებების პროვოცირება მოახდინოს (3).

ძილი მნიშვნელოვან როლს ასრულებს თავის ტვინში ახალი სინაფსური კავშირების ჩამოყალიბებაში, რაც აუცილებელია მეხსიერების პროცესირებისა და ფორმირებისთვის, ხელს უწყობს ზრდას, ტვინის დეზინტოქსიკაციას, იმუნური სისტემის გამართულ მოქმედებას, ჰორმონების გამოყოფას და საბოლოო ჯამში ჰომეოსტაზის შენარჩუნებას. ძილის ხანგრძლივობა შესაძლოა ეფუძნებოდეს გენეტიკურ მიდრეკილებებს, ცხოვრების სტილს, გარემოს ცვლილებებს და ამიტომაც ვარირებს სხვადასხვა ადამიანში. თუმცა, ძილის ფაზები (ძილის ნელ-ტალღოვანი ფაზა - DSWS, ან NREM და სწრაფ-ტალღოვანი, ძილი თვალის სწრაფი მოძრაობებით - REM) მონაცვლეობენ ყოველ 90-110 წუთში) (4). პირველი მათგანი 4 სტადიად იყოფა (5). სავარაუდოდ ძილის ამ მონაკვეთში

According to Stickgold, “When we dream, we get the pieces. When we wake, we can know the whole “(6).

Key words: Sleep functions, Diabetes, Cardiovascular disease, Obesity, Memory, sleep stages, dreams

Introduction

Sleep is an important part of our daily routine and we spend about one-third of our time doing it. Our bodies natural daily rhythms are regulated by structures in the brain that helps determine when we are fall asleep and wake up. Quality of sleep and getting enough amount of it at the right time is an essential to survival as food and water. Sleep physiology works best when the sleep pattern is correct. So, the best sleeping model is that person to fall asleep when the night comes and wakes up in the morning. Prolonged insomnia pushes person to brink of insanity and if it lasts too long, it can lead to death (7). Human can make decision about eating, drinking or breathing, while in the case of sleeping they cannot. The human behavior divides in two parts: simple and complex, and sleep is one of the most complex phenomena. As a result, Insomnia is much more complicated than sleep itself. Moreover, without sleeping we cannot form or maintain brain pathway which let us learn or create new memories and its harder to concentrate and respond fast (7). Scientist showed us sleeping plays a housekeeping role which removes toxins in the brain that build up when we are wake. Recent research described the lack of sleeping for a long period has a main effect on region of the brain which is responsible for memory, emotions, planning and language skills (3). Furthermore, seventeen hours of continuous awakening, giving a blood equivalent of 0.05% alcohol. Usually when people don’t have sleep, they lost the ability to respond quickly to the situation and make a decision or thinking logically. It is interesting to know that lack of awareness had a major role in many Great human historical such as Chernobyl incident or challenge Shuttle explosion. Also, lack of sleep leads to increasing the risk of high blood pressure and Nervous pressure. Researchers showed us being awake in prolonged time increase the risk of obesity because many hormones and chemicals that play an important role in controlling weight and appetite are released during sleep. Finally, as we figured out sleep has a varies functions and roles which all of them didn’t find yet (1).

ნეირონებს შორის სინაფსური კავშირები უფრო მძლავრი ხდება, მაშინ როცა სხეულის აქტივობები, სისხლის წნევა და გულის ცემა მცირდება. სავარაუდოდ ამ დროს ნანახი სიზმრები არ გვამახსოვრდება, ხოლო REM ძილი, რომელიც ელექტროენცეფალოგრაფიულად ღვიძილს ჰგავს [რისთვისაც მას პარადოქსულ ფაზასაც (5) ან სიზმრისეულ ძილსაც უწოდებენ] ხასიათდება გულ-სისხლძარღვთა და სუნთქვის სისტემების აქტივაციით, ზურგის ტვინის მოტონეირონების დეაქტივაციით, ხატოვანი და ხშირი დასამახსოვრებელი სიზმრებით. “სიზმრებში ჩვენ ნაწილებს ვიღებთ, ხოლო ღვიძილში, მთლიანობაში ვერკვევით“(6).

საკვანძო სიტყვები: ძილის ფუნქციები, დიაბეტი, კარდიო-ვასკულარული დაავადებები , ჭარბ წონიანობა, მეხსიერება, ძილის სტადიები, სიზმრები.

What is sleep?

Sleep is a natural process that occurs every twenty-four hours, During sleep several processes occur and many changes happen such as eyes closed, the muscles contraction and movement decrease also the breathing rate reduced, the Brain activities and waves became different and the important point is in sleeping the level of awareness decreased, reducing responsiveness to external stimuli (8).It is important to know that sleep is completely different from Coma, hibernation and death by the fact that it can be rapidly reversed. Sleep is characterized by certain patterns of activity of the brain that can be visualized using electroencephalography (EEG), and different phases of sleep can be differentiated using EEG as well. Also, sleep divides in two phases: NERM (non rapid eye movement) Which has 4 stages and REM(rapid eye movement). Sleep cycle occurs 3-5 times and each on is about approximately 90 minutes (8).

Anatomy of sleep

Sleep-wake cycles are controlled by different area in the brain which communicate with each other, some of these areas include: the Thalamus, Hypothalamus, pons, Pineal gland, Pituitary gland and Amygdala. Also, sleep is associated with the secretion of many hormones such as Melatonin, foliclestimulating hormone (FSH), Luteinizing hormone (LH), and growth hormone which is necessary for children (4).

The Hypothalamus contains a groups of nerve cells which act as control centers affecting sleep and arousal, in hypothalamus there is Suprachiasmatic nucleus (SCN)- clusters of many cells that receive information about light exposure from eyes and can control the behavioral rhythm (4).

The Thalamus plays as a relay center for information which are from the senses to the cerebral cortex(act in processing information from short memory to long term memory).In most sleep stages of sleep, the thalamus becomes quiet and allows the person turns off the external world, but during REM it becomes active and sending the cortex images, sounds and other sensations which make full our dreams(9).

The Brain stem communicate with the hypothalamus to control transition between waking and sleeping. In hypothalamus and brainstem there are sleep-promoting cells which can produce neurotransmitter(GABA).The GABA can decrease the level activity of arousal center in both regions(hypothalamus and brain stem).The other function of brain stem is in REM sleep, it sends signals to relax muscles which are important for movement. So, when they get relax ,we don't follow our dreams (10).

The Pineal gland which located between two hemispheres, Increase the production of Melatonin by the signals which is coming from SCN. Melatonin involves in the regulation of various biological rhythms and immune system. Moreover, it helps put the person to sleep once the light go down and it makes a sleep pattern for us (9).

The Basal forebrain located near front and bottom of the brain and when part of midbrain acts an arousal system, it promotes sleep and wakefulness. In this region there are cells which release Adenosine that supports sleep and when people use Caffeine, they block the activity of this molecule. (11)

The pituitary gland during sleeping secrets FSH and LH which are essential for reproductive system and also secrets growth hormone that has a role in physical growth and maturation (11). The Amygdala involved in processing emotions and increase the activity during REM sleep.(11)

The Internal clock (Circadian rhythms)

The circadian rhythms is a natural, internal system which tell the body when to sleep, wake and eat over 24 hour period. Also, it is influenced by light exposure and temperature. It is controlled by a group of neuron cells (suprachiasmatic nucleus) which locates in Hypothalamus. The receptors in the eyes detects darkness then transfer signals along the suprachiasmatic nucleus and stimulate the production of melatonin (sleeping hormone) (6).

Sleep phases

The sleep has two main stages: Quiet sleep or non-REM sleep (NREM) and Dreaming sleep or (REM sleep). The NREM by itself divides in four stages. These two types of sleep are described alternately by differences in eye movements, muscle strength, heart rate, blood pressure (BP), breathing patterns, brainwave activity, and dreaming. Also, in all sleep stages we can see dreams, but those ones which people see in NREM, will become forget and dreams that are seen in REM will not

become forget. Moreover, in the brain there is a structure named Habenular in the brain, which on the NERM phase prevents the formation of memory (12). In some diseases this structure, is affected and has problem, so person can remember incidents that were seen in NREM and cannot recognize them that events were seen in dreams or reality (12).

NREM

Quite sleep or NREM is an important type of sleeps which can control the brain and body movements and it consists 80-85% of sleep. In this state, the brain is calm, but the body moves. At this time, hormones are released and enter the circulatory system, and the body repairs the fatigue and burnout caused by daily activities. During NREM the coordination between neurons become much stronger, as a result of this coordination, the frequency of brain waves decreases and the amplitude of these waves increases (12).

Stage 1: Is the transition state from wakefulness to light sleep. It takes a few minutes several minutes and the brain waves become slow and from Alpha changes to Theta waves. In this stage the body temperature decreases and eye movements, heartbeat, breathing slow and muscles get relax. It includes 2-5% of sleep. The first stage of sleep is the lightest stage. If we wake up at this stage, we will probably feel that we have not slept at all (12).

Stage 2: At this stage, we can still wake up easily and without feeling confused. After 10 minutes of light sleep, real sleep begins, it lasts about 20 minutes. In addition, the brain's electrical activity is irregular, in EEG activity and maximum Theta waves are observed. At this time, we have large, slow waves intermingle with brief bursts of activity called sleep spindle, when brain waves speed up for roughly half a second or longer. Scientists showed when spindle happens, we disconnect from outside sensory and start the process which organize memories for long term storage. Moreover, at this stage we have the other phenomena called K complex. K complex is the result of increasing the short period of brain activity which

by itself as a result of external stimuli such as the noise, or internal stimuli such as leg cramps. Also, at this stage, more intense stimuli are needed to stimulate and excite person to wake up. The heartbeat and breathing slow, and muscles relax even further. Also, body temperature drops and eye movements stop (13).

The stage 3 and 4 compose deep sleep and Theta and Delta waves are registries.

Stage 3: It occurs in longer periods during the first half of the night. Heartbeat and breathing are at the lowest level during sleep and muscles are relaxed, so it is difficult to awaken a sleeper. At this stage the brain starts to generate low frequency (slow) Delta waves. Stage 3 usually lasts only a few minutes and is moved to step four, which lasts 20 to 40 minutes at the end of the cycle (13).

Stage 4: Stage four is the deepest stage of sleep. It is known for its rhythmic breathing and limited muscle activity. The stages that are difficult to wake up from. Only loud noise wakes the person from this stage of sleep, and person does not feel complete arousal and is confused. At this stage the slow Delta waves are generated. Moreover, children's nocturnal enuresis, nightmares, and sleepwalking occur (13).

Those stages take 80-90 minutes which form the NREM then REM phase begins when the brain is completely active. During REM sleep the EEG appears to be similar to stage 1 NREM sleep, or wakefulness. REM phase occurs about 90 minutes after falling asleep. Eyes e rapid movement is observed (14). The brain waves have low frequency and become fast similar to wakefulness. Also the breathing becomes much faster and the heartbeat increase, the Sympathetic activities increases and the amount of Acetylcholine in the brain is elevated, but the amount of Noradrenalin and Serotonin decrease, muscles are temporarily paralyzed, it happens because the sleeper sees dreams when motoneurons in the spinal cord are inhibited (14). In different ages the concentration of REM and NREM are differ. After 65-70 the deep sleep decrease even close to zero. In addition, REM sleep named Paradoxica sleep because the brain is completely active, it likes rebuilding itself and the metabolic and electrical activities are high, but the muscle tones is low. Moreover, poikilother-

mia is described at REM phase. The brain blood flow and brain oxygen consumption are too much. Further at late night the concentration of REM is increased. Some significant events happen simultaneously. First, at the beginning of morning REM has high concentration, second,

the body temperature is very low. In depressive patients' low level of mood mostly depends on the intensity and frequency of REM sleep. As a result, there is a connection between body temperature, REM sleep and mood. It is interesting, that before ovulation women have minimum body temperature and get depressed. Finally, these three parameters have connection with each other and REM sleep deprivation can be used as a way for depression treatment (13).

The role of REM sleep

Deep sleep restores the body, scientists believe that REM or dreaming sleep restores the mind, perhaps in part by helping clear out irrelevant information, stimulates the central nervous system and earlier studies found that REM sleep facilitates learning and memory. A lack of REM sleep may have adverse implications for physical and emotional health. Also, it is also thought to contribute to brain development in infants (14).

How Much Sleep Do You Need?

This question doesn't have clear answers because the amounts of sleep among people are different, but we can say the amount of sleep each person needs is such that if provided, they will not feel drowsy the next day. Also, during aging the sleep pattern change, for example babies initially sleep as much as 16-18 hours per day, which needs for growth and brain development, children and teens on average need 9.5-10 hours of sleep per night and most adults need 7-9 hours, while after 60 sleep tends to be shorter, lighter and interrupted by multiple awaking because of that elderly people tend to take medications to have a regular sleep pattern (16).

Function of Sleep

It has several essential behavioral and physical functions. The lack of sleep for prolonged time of wakefulness, leads to emotional instability, decreased pain tolerance, metabolic disease, deficiency of immunity and impaired memory consolidation (2).

Memory

Sleep has a major role in the integration of memory and select the important information. Researcher believed that it helps brain to sort information or specific details. In addition, sleeping helps to clear out toxins which accumulate in the brain when we have normal activity during day. They mentioned a relation between Alzheimers disease and brain toxins. Many researches showed Beta-amyloid is a protein associated with this disease. During sleep, channels in the brain open and allow the flow of cerebrospinal fluid (CSF) to clear debris which likes the lymphatic system function (17).

Physical Health

Sleep is so essential for body specially for repairing system. It helps for hormone regulation such as Leptin which regulates feeling of hunger and fullness, so, it has directly connected to Obesity. Another hormone is insulin that is responsible for regulation of glucose in the blood. As a result, lack of sleeping causes to Diabetes. Moreover, chronic sleep deficiency has a connection with cardiovascular disease, stroke and kidney disease. The immune system functions is related to sleeping, if its not sufficient and doesn't have quality, it becomes weakness and increase the risk of sickness. Further, in children it has a main role for growth and also, growth-promoting hormones that increase the rate of repair cells and tissues in the body (17;18).

Metabolism and sleep

Basically, metabolism regulation is controlled by sleeping which in turn acts as a restorative function. Many genes have main role in metabolism and their regulation happens during sleeping. Also, protein synthesis occurs more in sleeping rather than wakefulness, as a result sleep deprivation enhances brain mRNAs that modulate glycogen metabolism and glycogen synthesis (2;18)

Conclusion

Sleeping is part of a cycle called the sleep-wake cycle. In contrast to waking up, which is the time of mental activity and energy consumption, sleep is a time when the mind and passive physical function are being revived. Also, it can be regulating globally, locally and regionally. Typically, sleep and wakefulness have a cycle which is called circadian cycle that is created during 24 hours of light-darkness. The circadian is controlled by suprachiasmatic nucleus in Hypothalamus. Additionally, it is thought Pineal gland secrets Melatonin hormone, which helps the regulation of circadian cycle. Also, Sleep has 2 main phases: NREM or non-rapid eye movement and REM or rapid eye movement. The first one (NREM) is a quiet sleep and the brain is almost inactive, but still control-

lable. This type of sleeping has 4 stages which shows the depth of sleeping (1;4;6). The first stage is the short transfer phase, which occurs at the beginning of sleep when a person feels comfortable. Step 2 is a deeper sleep and it takes about 10 to 25 minutes, and EEG activity by the sleep spindle involves a sudden and slight increase in the frequency of the waves. Stages 3 and 4 indicate deep sleep during which the muscles of the body are in a more relaxed state and the heart rate and blood pressure decrease and the function of the digestive system slows down. After NREM REM phase usually begins. REM sleep is associated with rapid eye movements, decreased muscle movement, and clear dreams. External sensory data is prohibited, while internal sensory data such as visual and auditory systems are felt (14).

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