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Review

NEUROPHYSIOLOGICAL BASIS OF DREAMING – A REVIEW

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ABSTRACT
The main purpose of this review paper is to summarize and analyze the current information of the essence of dreams as an important part of the normal sleep and neurophysiological mechanisms of their regulation. Described in details are the dreaming in NREM and REM sleeping periods and the role of mesocorticolimbic dopamine system, cholinergic system and visual cortex. In addition, some aspects of neuropsychological basis of dreams and dreaming in animals are also discussed.

Key words: REM dreaming, NREM dreaming, essence of dreams, neurological control of dreams, dopaminergic and cholinergic system

INTRODUCTION

It is known that adults spend approximately one third of the day in sleep, that is, about 7-8 hours. Of course, these are average data, since the sleep time for newborns and children is much longer, 10-12 hours, and with time it decreases so that at around the age of 20 it reaches the values of adults. If we relate these data to the average duration of human life between 75 and 80 years. Therefore, a person spends approximately one third of their life in sleep, that is, about 25-30 years, of which - 6 years in dreaming. The question is why sleep is necessary and is it really a waste of time. For a long time sleep was considered a completely passive process of temporary loss of consciousness, during which nerve cells restore their normal working ability and functional activity. In the last few decades, however, with the development of neurophysiology and electrophysiology and the use of electroencephalography, electromyography, electrooculography, nuclear magnetic resonance, computed tomography, etc. it has been indisputably proven that sleep and dreams are processes of high functional activity of nerve cells, comparable to that of the state of being awake. This applies mainly to one of the phases of sleep, namely paradoxical or REM sleep, when most of the dreams, i.e. 90-95% occur (1-4). The electroencephalogram shows that beta waves dominate during this phase, as is the case during wakefulness. Therefore, now the sleep, including dreaming, can be defined as a continuum of consciousness, because during this period the recovery and restoration of nerve cells are accompanied by very important processes, such as filtration and distribution of information, memory storage, cognitive capacity of the brain, as well as an involvement in the control of normal functions of the endocrine system and immunity (1). Moreover, new studies have revealed a causal link between sleep disorders and different serious health problems, including obesity, insulin resistance, type 2 diabetes mellitus, cardio-vascular diseases and depression (1).

Recently, in a review paper we described in detail the current knowledge on the neurophysiological mechanisms of regulation of wakefulness and sleep, including types of sleep (non-rapid-eye-movement (NREM) sleep and rapid-eye-movement (REM) sleep), brain waves, sleep architecture, circadian and

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homeostatic regulation of NREM and REM sleep and the role of melatonin in particular (1). Special attention was paid to the pharmacological aspects and the use of some new classes of sleep promoting agents – melatonin, melatonin receptor agonists and orexin receptor antagonists. Little is known however, about the physiological meaning and control of dreams. Therefore, the main purpose of the review is to summarize and analyze the current information of the essential of dreams as an important part of the normal sleep and neurophysiological mechanisms of their regulation.

ESSENTIAL AND NEUROPHYSIOLOGICAL REGULATION OF DREAMING

In recent decades, it has been established and affirmed that dreams are the product of the work of two main systems - the mesocorticolimbic dopamine system and the visual cortical system (2). The first is considered as the primary basis. In modern neuroscience, a distinction has been made between the mechanisms underlying REM sleep and those responsible for dreaming (3). The main arguments for this have been obtained from patients with damage to the structures controlling REM sleep (the pontine-brainstem) - such patients do not lose the ability to dream. When one of the two mentioned areas, underlying the occurrence of dreams are damaged, the latter are lost and REM sleep is preserved (4, 5). In addition, dopamine agonists and antagonists can influence dream quality without affecting REM frequency and duration. In other words, REM pathways are only one way of inducing dreams, and the two can be observed independently of each other. Local stimulation of the hindbrain, not only during REM but also during NREM sleep, can induce dreaming.

It turns out that dreams have more to do with memory, emotions, and consciousness, than with a specific sleep phase. Although much more often dreaming occurrs during REM (90-95%), it is not typical only of this stage of sleep, i.e. 5-10% of awake people, during NREM sleep, remember their dreams (6). In his study, Foulkes (7) makes a convincing argument against critics who believe that NREM dreams are actually misidentified REM dreams. He states that waking up immediately after falling asleep, during drift or so-called first and second phases of NREM in 70% of cases there are memories of dreams. These stages of sleep occur long before entering REM sleep and are therefore strong evidence in support of NREM dreams. There are also reports of NREM dreams at the end of sleep, in the ascending part of the pre-awakening hypnogram, after the last REM phase (8). Moreover, these transitional phases differ dramatically from REM sleep in terms of the physiological mechanisms underlying them. These correlate with increased levels of norepinephrine and serotonin, and decreased levels of acetylcholine, while the case during REM is exactly the opposite. In addition, 5-30% of people awoken during REM sleep report that they were not dreaming. Therefore, there is dreamless REM sleep and non-REM dreams (9). Dreams do not occur in a certain phase of sleep, but at a certain level of brain arousal, regardless of REM or NREM (10). This level of brain activity resembles the waking state and occurs during both REM and NREM sleep. Originally, this theory was associated with general brain activity in the initial entrainment phase, when the brain transitions from wakefulness to sleep, and at the end of sleep, when the brain prepares for wakefulness. During these phases, as well as during REM, the brain is active and this creates conditions for dreaming. Later, however, the theory was revised, and now it is known that it is a question of activation of certain areas.

A strong boost in the understanding of dreams was given by the development of imaging techniques. With the help of PET tomography and fMRI, areas of increased or decreased activity during dreaming can be examined. Significant findings were made by Braun et al. (11) who, using functional magnetic resonance imaging, examined brain activity during REM sleep, because this is when dreams are most likely to occur. The parts of the brain that showed the highest activity during dreaming were the limbic system and most of the visual cortex. This discovery is in contrast with the so-called activation synthesis theory, according to which ascending impulses from the brainstem during REM sleep would lead to the chaotic activation of non-specific areas in the cortex and subsequently to the generation of dreams. The specific structures that showed increased activity were the medio-basal prefrontal lobes, the thalamic nucleus, the pontine tegmentum, the anterior cingulate gyrus, the amygdala, and the hippocampus. Sometimes the primary visual cortex and the dorsolateral prefrontal cortex remain inactive during REM (11), considered by Yuval Nir & Giulio Tononi (12), as a likely reason that often humans cannot recall their dreams in the morning. The prefrontal cortex is involved in memory processes. Partial deactivation of cortical prefrontal regions during dreaming facilitates the emergence of emotional contents belonging to subcortical and limbic structures, allowing self-regulation and better emotional balance during wakefulness (13).

In their studies, Siclari et al. (14) talk about the presence of the so-called "hot spot" in the posterior cerebral cortex involving the medial and lateral occipital regions. Through high-density EEG (256 channels) and a series of awakenings at different times of the night, during NREM and REM, they reported that dreaming occurs when there is a decrease in the activity of slow low-frequency waves (1-4 Hz) and when sleep spindles occur with increased frequency. The absence of activity in this area is also associated with a lack of dreams. They also found that high-frequency activity in these areas correlated with specific dream content such as thoughts, sensations, face recognition, spatial orientation, movement and speech. In a subsequent study, Siclari et al. (15), have observed very high and steep slow waves during NREM sleep, followed by increased activity of high-frequency (10-30 Hz) waves (K-complexes) in the frontal cortex, defined as "microarousals", which they associate with successful recall of dream content after awakening from REM. During REM sleep because of the inactive frontal and parietal lobes the dreamer may experience a false sense of wakefulness. These neural areas are responsible for memory during wakefulness and self-awareness, as well as insight. Nonetheless there are certain aspects of consciousness accessible during REM because of the active areas, such as pontine tegmentum, amygdala, anterior commissure, parietal operculum, thalamus and frontal white matter, which are inactive during NREM (16). Therefore, the experience of dreams and their subsequent recall occur by two separate mechanisms (17). Carhart-Harris, R.L. (18) and Mota et al. (19) speak of sudden phasic high-amplitude slow theta waves, in the 4-8 Hz range in limbic structures, during dreams. A characteristic hippocampal theta rhythm has also been reported during REM in cats, rabbits, and rats, as well as outside REM (20).

A state known as lucid dreaming has been described, where individuals are aware of their own consciousness. It is a rare and uncommon experience and typically occurs during late-night REM sleep periods. Although it is considered as an REM feature, lucid dreaming may also occur during NREM. Dream lucidity can be trained and the dreamer can learn to give signals when identify a lucid dream. Depending on that it can vary from achieving slight control of consciousness to actively and volitionally navigate through the dream storyline. According to this, Mutz, J. & Javadi, A. (16) consider lucid dreaming as promising avenue for research into dreams and consciousness. As D'Agostino et al. (21) summarize the implications of dream and consciousness, research is multiple, and forms an essential part of psychiatry. Knowing the brain basis of dreams and lucidity may help to understand why psychotic patients lack insight; why hallucinations occur even without neurological lesions in the brain; what is the neurological foundation for long-term of sudden disconnections from reality seen in various psychotic conditions; and last but not least to throw light on neuromodulatory mechanisms of psychotropic medications by their specific effects on dreaming.

Dreams occupy about 20-25% of the time spent in sleep. They occur during each of, typically 4 to 5 over 90-minute cycles comprising all phases of NREM followed by REM sleep (22). Apart from REM, reports of dreams have been found during all phases of NREM, especially at the onset of sleep and in the earlier hours of the morning. Dream frequency increases as REM periods lengthen at night, being longest in the early morning. They are characterized by the presence of different sensory modalities such as visual, auditory, motor, tactile, olfactory and gustatory elements. Visual sensations are almost always present, followed by auditory ones (23). Motor and tactile perceptions are less frequently described, and only 5% of dreams include olfactory and gustatory ones. These data directly point to the activation of the corresponding cortical areas during dreams. Activation of the amygdala and insula, and hence fear, explains the high frequency of dreams, waking feelings of stress, fear, and threat (24). The ability to recognize faces during dreams is due to the involvement of the fusiform face area, the amygdala, the posterior temporal cortex, and the prefrontal cortex. Lesions in the occipital gyri lingualis et fusiformis can lead to a lack of colour perception during dreaming.

As the night progresses, circadian activation of the cerebral cortex begins, which changes the nature of dreams (25). NREM dreams in the entrainment period, phase N1, contain mostly positive friendly interactions, self-related information, and actual waking life events, while as sleep progresses, they begin to become more lucid, containing symbols and metaphorical references, and are more emotionally attached. REM dreams are more likely to contain negative and antagonistic interactions than NREM, and there is less integration between self-awareness and social reasoning with an autobiographical element (26). There is significantly greater activation of the amygdala and other structures of the limbic system compared to NREM (27), so the expression of instinctive emotions and behaviors, such as fear and aggression is more prevalent in REM than in NREM dreams. In their research, Martin et al. (28) convincingly demonstrated that REM dream reports have greater structural connectivity and are therefore more complex than NREM N2, and this is independent of dream duration. In addition to that, there is a strong activation of the basal ganglia during REM sleep which may mediate the widespread fictive motion experienced in dreams. The connection of the basal ganglia with brainstem nuclei and cerebellar vermis may contribute to a feeling for motor control during REM and vestibular sensations interpreted as flying or falling (29).

ROLE OF MESOCORTICOLIMBIC DOPAMINE SYSTEM

This system begins in the ventral tegmental area of the midbrain. From there, neurons continue through the dorsolateral hypothalamus into the midbrain and terminate in the nucleus accumbens, giving multiple projections to the anterior cingulate gyrus, amygdala, and frontal lobes (29). This system is also called the “SEARCH” system and its primary neurotransmitter is dopamine. It is involved in the behavior of reward, the instinct, by supplying the energy and excitement for the satisfaction of the so-called "appetitive" urges (hunger, thirst). It is also associated with aggressive behavior such as predation. In other words, dreams are provoked and generated by emotional and motivational stimuli. Moreover, research indicates that dopamine, in addition to a role in dream production, is also involved in the induction of REM sleep (2). Dopamine, however, is not the only neurotransmitter in the SEARCH system. Glutamate, GABA, serotonin, acetylcholine are also involved. They directly and indirectly affect the effect of dopamine. This indicates that the SEARCH system interacts with other systems, such as memory systems. Thanks to them, we actually learn from our experience.

Overstimulation of this system (by psychotropic substances) can lead to the appearance of schizophrenic symptoms, but in addition, such patients report vivid, realistic dreams and an increased frequency of nightmares, with no effect on the duration and frequency of REM sleep. i.e. this dopamine system is specifically related on the one hand to dreams and on the other - to conditions, such as schizophrenia. It is also a main target for antipsychotic medications, as one of the effects of this treatment is a loss of interest in the surrounding world and an inability to concentrate attention, precisely due to blocking neurotransmission in this system (30). Disturbances in the mesocorticolimbic system underlie addiction and depression (31).

ROLE OF VISUAL CORTEX AREA

Visual areas, which play an essential role in dreaming, have been accepted as a secondary driving force, after areas in the prefrontal cortex involved in the mesocorticolimbic system. Solms (32) found that unilateral and bilateral local lesions of the occipital-temporal-parietal (OCT) junction lead to the loss of various features of visual imagery during dreaming, for example colour perception or movement. The same author reports that the right OCT region is responsible for spatial thinking, while the left one is responsible for abstract, symbolic thinking. During wakefulness, projected objects on the retina are transmitted to the visual cortex following the sequence described. The primary visual cortex is the first area, where the information from the vision analyzer comes in. It is responsible for visual perception, and its absence leads to cortical blindness. Such patients lack visual sensations. In front of this area is the area for object and face recognition, colour processing and motion. Therefore, when it is affected, the processing of this type of information stops, even in dreaming. Most rostral in the visual cortex is the third area, which has the highest level of processing of incoming information - abstract thinking, functions such as writing, calculation, construction and spatial orientation. This is the "output" of the system, the final unit for processing the information flowing from the retina.

During dreaming, however, Solms (33) points out that this hierarchy is reversed, i.e. the flow of information flows in the opposite direction - from the third to the first zone. This is because damage to the first zone does not lead to any changes in dreams, therefore it is not the "input" unit, but becomes the "output" end. While disorders in the third, occipital-temporal-parietal connection, terminate the ability to dream completely, i.e. the processing of visual information starts from this part of the visual cortex. This is the so-called "regression model" first introduced by Freud.

NEUROPSYCHOLOGICAL BASIS OF DREAMS

From the above-mentioned, it follows that dreams are not the result of chaotic diffuse activation of neurons in random areas of the brain. Dreams are the product of the work of a certain structural network of cells in precisely defined areas in the brain. This characteristic of dreams suggests the presence of consistency and meaning in this phenomenon. Otherwise, why does our brain need to coordinate its actions if it is aiming for an arbitrary result? It is widely accepted among neuropsychologists and psychotherapists that dreams symbolize subconscious questions and conflicts (33), which in the waking state remain hidden due to the presence of the so-called "ego-defense", but during sleep they are realized in consciousness through dreams. Freud considered the interpretation of dreams to be the key to unraveling many psychological problems, precisely because, according to him, dreams help us become aware of what is hidden in our minds. Often, however, this "surfacing" of information takes the form of too bizarre, atypical and not at all literally reflecting the meaning carried by objects and plots that play out in our consciousness while we sleep.

A number of scientists and researchers devote much of their work to this area. Clara Hill (34), a clinical psychologist, produced more in-depth work on dream interpretation, working with dreams in psychotherapy, which reveals her view that dreams give literal or metaphorical expression to our emotions. Other researchers are: Matthew Walker (35), who wrote the book “Why We Sleep: Unlocking the Power of Sleep and Dreams”; Tononi & Cirelli (36): “Sleep and the Price of Plasticity: from Synaptic and Cellular Homeostasis to Memory Consolidation and Integration”. However, there is no universal dictionary for interpreting dreams - the same object can have a different, individual meaning for each person. Apparently, the conscious and subconscious interact in a way that cannot yet be figured out. Jung believed that dreams are "a spontaneous self-portrait in a symbolic form of the actual situation in the unconscious. They invariably seek to express something that the ego does not know and does not understand."

According to Cartwright's (37) theory, dreams perform a regulatory role. They can serve also as an “emotional thermostat” (38). It informs us that an imbalance has occurred which disturbs the state of homeostasis in our body. If dreams have successfully fulfilled their role, the emotion cannot enter our consciousness and is not remembered, thus protecting the dream and dissipating the emotional charge from the experience, preparing the dreamer to wake up in a positive mood. In other words, the attempts of our subconscious mind to find a solution to a given problem have ended successfully, which ultimately leads to our adaptation. If the problem is not resolved, dreams begin to be filled with negative context. The presence of such dreams indicates that we are not able to connect past memories with a present problem that is embedded in us and it has remained unresolved. Such unresolved conflicts lead to disturbances and lowering of mood, and this is also reflected in dreams. Patients diagnosed with depression show a dramatic decrease in dream frequency, which, combined with the depressed post-sleep mood in these individuals, suggests that they fail to effectively activate past memories during dreaming and subsequently fail to integrate the effect of this in the neural networks of the long-term memory during sleep. They wake up depressed, with a depressed mood, which suggests that dreams have not been able to fulfil their regulatory role. Generally speaking, dreams attempt to restore emotional balance within us. Their function is to dissipate and reduce the emotional saturation accumulated in our subconscious during alertness, successfully integrating information from new and old memories and storing it in long-term memory, which subsequently makes it possible to develop new patterns of behaviour. In this way, there is a better provision and preservation of the well-being of the individual (39).

DREAMS AND MEMORY

It is widely believed that dreams aid memory processes, particularly learning. According to consolidation theory, memories are consolidated or stored in long-term memory during dreaming (40). During dreaming, activation of the hippocampus is observed, which is of primary importance for actual memory, or the so-called in "episodic memory" in neuroscience. This is when we consciously recall past events that are important to our lives. Reactivation of neurons in the frontal cortex, which is involved in retrieval, the very process of returning episodic memories to consciousness, in a certain systematized and rational organization corresponding to the requirements of reality, has also been established during dreams (3). When these systems are reactivated during NREM, it is related to the consolidation of declarative memory – remembering names, dates, places, facts, events (41). When reactivation occurs during REM sleep, it has a positive effect on procedural memory – learning motor skills about how to do something, such as tying shoes or riding a bike (42). In fact, dreams are considered to be a conscious realization of memories in the process of memory consolidation. A seminal study in this regard was done by Wilson, M.A. et al. (43) who tracked the coactivation of cells in the hippocampus of rodents placed in laboratory conditions to actively seek an exit from a maze. They found that during NREM sleep in these rodents, the same neurons were activated in a preserved temporal sequence as during wakefulness. In similar studies, these conclusions were later also confirmed by others (44, 45, 46). More than 80% of our dreams contain facts from previous real-life memories (47, 48, 49), and 50-70% of them are from the previous day, and this has a positive effect on learning, memory and solving real-world tasks (40). During the first phase of NREM, after falling asleep, dreams of more recent experiences are common, while during deep sleep and REM sleep, dreams combine moments from the individual's more distant past (19, 50). This repetition (reactivation) of neural pathways underlies long-term memory formation.

The actual neural mechanisms underlying memory and dreams are not limited to simple repetition. Thanks to the complex inter-neural relationships, the dense neural network and the pronounced plasticity of the synapses in the brain, in addition to simple repetition of past experience and its memorization, an evaluation of possible expected events in the context of the same experiences, but without actually having been studied during of cheerfulness. Inclusion of new neural pathways in the same area, in addition to previous ones based on past experience, has been observed, with which the brain can anticipate other possible solutions to a task before a specific behavioral response is produced, and these processes occur both in the awake state and in the sleep time (51, 52). It is very likely that the so-called "*Déjà vu* phenomena" in which there is a re-experiencing of past events for a short period of time.

DREAMS IN ANIMALS

The difficulty in using animals as a model in dream research is obvious – the impossibility of verbal communication in the presence or absence of animals after waking up. However, this should not be the only possible way to obtain this information. That is why the latest discoveries in neuroscience are directed precisely at the search for those processes in the brain that are a sure sign of the progress of dreams. From the exposition so far, it has become clear that such mechanisms exist. And their proof is convincing by methods with lesions in these areas, which lead to the cessation of dreams or the absence of memories of them. Even if we cannot speak for sure about self-awareness in animals, they still possess a primary awareness of the things that surround them - such as sensory perceptions, experiences, cognitive or memory-based recognition. In other words, animals possess the necessary prerequisites for this type of dreams (53). Another circumstance in support of this is the presence of motor acts during sleep. Reduced, but not completely absent, muscle tone allows performing various limb movements imitating running, stalking and attacking prey, grooming. Data for the examples shown were recorded by Hendricks et al. (54) in cats. Similar research was conducted by Sanford et al. (55) in rats, and numerous YouTube videos of dogs running in their sleep are also available to the general public. Meisel et al. (56) published interesting papers related to the behavior of octopuses during sleep. Sleeping octopuses sometimes exhibit twitches or contractions of tentacles and suckers, increased breathing and eye twitches, rapid changes in body color unrelated to their sleeping environment.

Future studies using animal imaging methods similar to those of Siclari et al. (14,15) in humans, for a correlation between the activity of certain brain structures and specific dream content would be of great importance in clarifying the question of whether animals really dream.

CONCLUSION

Dreaming is a phenomenon that still hides many unknowns. However, advances in neuroscience are opening up to us a whole new view of how our brain works and how far the limits of its capabilities are. Dreams are a completely different world from the physical one we know. They are a bridge to the understanding of the human mind, in which neuropsychology and psychoanalysis have been devoted since the dawn of mankind. They are also a bridge between the consciousness and the subconsciousness. They represent a key to getting to know our inner world and are a valuable assistant in dealing with temporary disturbances and difficulties. It seems that humans possess mechanisms for the regulation not only of their material substrate (cells, tissues, and organs), but also of that part that has no material manifestation, which is believed to be located in the brain and is briefly called simply "mind".

Dreams have a structure - they are formed by the work of two functionally related areas in the brain - the mesocorticolimbic, considered primary, and the visual area. The main neurotransmitter in the process of dreaming is dopamine, which shows that dreams are provoked by emotional and motivational stimuli, and the flow of information in the visual cortex during dreaming is on the principle of "reverse projection" in relation to the same in the waking state, this input becomes output during dreaming. Dreams bear the character of experiences in waking life. They underlie the integration of new information with already accumulated past experience and the utilization of these new interconnections in the individual's long-term memory. Sleep has a role in shaping the qualitative and quantitative characteristics of dreams. REM dreams differ from those during NREM. They are more consistently connected, have greater complexity and duration. They carry a stronger emotional focus and elements of symbolism. During dreaming, the same neural pathways that were intensely excited during wakefulness are activated, in order to carry out the processes of memorization and learning. Based on this repetition, new neural trajectories are also included, the role of which is to simulate expected experiences and enrich the so-called. a "cognitive map" through which different patterns of behavior are worked out.

Dreams related to primary conscious actions, such as sensory perceptions, experiences, cognitive or memory-based recognition are probably not unique to humans, because a wealth of research involving experimental animals shows that the same mechanisms of sleep and memory are available in them. The motor acts that our pets perform during sleep are very likely to suggest dreaming.

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