

### A Probable Cell Model in the Creation of Dream Scenarios: Review

### Rüya Senaryolarının Oluşmasında Olası Bir Hücresel Model

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Yazışma Adresi/Correspondence: Lamia PINAR Gazi University Faculty of Medicine, Department of Physiology, Ankara, TÜRKİYE/TURKEY Ipinar@gazi.edu.tr ABSTRACT Dreams are the scenarios that develop as a result of the random relationships established between the neuron groups constituting the memory of various events, peoples and objects. In rapid eye movement (REM) period of sleep, the stimulations (bursting activity) sent by the pontine reticular formation, also stimulate the neuron's pools of the memories in the neocortex and other memory storage areas of the brain constitute the dream scenarios. The bursting activity (discharges) from those pontine geniculo-occipital (PGO) generating cells reach to the occipital cortex, entorhinal cortex, piriform cortex, amygdale, hippocampus, and many other thalamic, hypothalamic, and brainstem nuclei. The functional relationship between amygdala, hippocampus, thalamus, hypothalamus, orbito-frontal cortex and anterior cingulate make up the limbic system which provides the emotional aspects of dreams. The axon of each neuron in the central nervous system is divided into thousands of axon branches, on average. These axon terminals establish thousands of synaptic relationships within the related neuronal pool. If the neuronal connections of recently-stimulated memories establish random synaptic relationships with each other it can be concluded that activated neurons can randomly stimulate the neurons of other memories converging on them or at least facilitate the stimulation of these neurons. Thus the memory neurons related to the people, events or subjects that have occupied the mind in recent waking activities (for example, grandmother neurons) may stimulate other memory neurons (for example, an armed conflict) randomly and independently. So without subject integrity, these components of memories constitute a dream scenario (a grandmother with weapon).

Key Words: Dreams; sleep, REM; brain stem; nerve net

ÖZET Rüyalar çeşitli olaylar, insanlar ve objelere ait belleği oluşturan nöron gurupları arasında kurulan rastlantısal ilişkilerin sonucu gelişen senaryolardır. Uyku sürecinin hızlı göz hareketleri (rapid eye movement, REM) fazında pontin retiküler formasyondan başlayan uyarılar (bursting activity), aynı zamanda neokorteks ve diğer bellek depo alanlarında bulunan nöron havuzlarını da uyararak rüya senaryolarını oluşturur. Bu pontin genikulo-oksipital (PGO) kaynaklı hücre deşarjlarının ulaştığı en önemli yapılar, oksipital korteks, entorhinal korteks, piriform korteks, amigdala, hipokampus ve diğer pek çok talamik, hipotalamik ve beyinsapı çekirdekleridir. Amigdala, hipokampus, talamus, hipotalamus, orbito-frontal korteks ve anteriör singulat korteks arasındaki ilişkiler, rüyaların duygusal yönünü oluşturan limbik sistemi yapar. Santral sinir sisteminde her bir nöronun aksonu ortalama binlerce akson dalına ayrılır. Bu akson terminalleri, ilgili nöronal havuzlar içinde binlerce sinaptik ilişki kurar. Böylece, eğer son zamanlarda uyarılmış bir belleğin nöronal bağlantıları diğer bazı bellek nöronları ile rastgele sinaptik bağlantılar kurmuş ise, aktive nöronların rastlantısal olarak konverjens yaptıkları bu bellek nöronlarını da uyarabildiği yada en azından uyarılmalarını kolaylaştırabildiği ileri sürülebilir. Böylece, son zamanlarda, uyanık iken zihni meşgul etmiş ve uyarmış bir kişi olay veya cisme ait bellek nöronları (örneğin anneanne nöronları), rastlantısal ve bağımsız olarak başka bellek nöronlarını (örneğin bir silahlı çatışma) uyarılabilir ve bir konu bütünlüğü olmaksızın bu bellek parçaları rüya senaryosunu (silahlı anneanne)

Anahtar Kelimeler: Rüyalar; uyku, REM; beyin sapı; sinir ağı

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he brainstem not only generates the rapid eye movement (REM) period of sleep, but also enables dreaming. In the REM phase, sensory inputs and motor stimulus in the brain cease and the prefrontal cortex is stimulated only by the brain stem. So perception turns to the internal domain or endogenous cerebral activity while sleeping. Pontine reticular formation is involved in the cholinergic initiation and/or maintenance desynchronized sleep and that the mid-brain reticular formation mediates arousal. The mechanisms responsible for the generation of the dream scenarios still remained largely unknown.

Sigmund Freud started the dream interpretation as a scientific research and used it in the psycho-analysis in the end of 19th Century. For Freud, dreams were disguised wish-fulfillment, an unconscious way for us to express our sexual and aggressive fantasies, which are forbidden while we're awake. Freud claimed that dream was not coincidental. The symbols manifested in dreams were, in his opinion, more or less sexual and these symbols were the subconscious desires and fears of the dreamers about sex.4 Another very famous dream theorist was Carl Gustav Jung, who lived at the same period with Freud and was impressed from him firstly. But then Jung disagreed some of the Freud's theories, and influencing from metaphysics, tried to show the close paralelles between ancient myths and dreams. Jung proposed that the concept of introversion and extroversion, the concept of complexes, the concept of collective unconscious influence our contents of dreams.<sup>5</sup>

Recently the most generally accepted dream theory was offered by Hobson and McCarley (1977). Due to Hobson and McCarley, dreams are meaningless and random. When the forebrain is confronted by the resulting bizarre array of random visions and thoughts, it attempts to synthesize them into a coherent or semi-coherent story. Hobson and McCarley's theory named "activation-synthesis hypothesis" offers an explanation of dreaming based on the physiology of REM sleep. According to this hypothesis, dreams are the result of the forebrain responding to random activity initiated at the brainstem. This is demonstrated by the ponto-geni-

culo-occipital (PGO) waves that occur during REM sleep. According to Hobson and McCarley this random activity, emanating from the pons, passes through the lateral geniculate nucleus of the thalamus which is the area through which sensory information passes and occipital areas where visual information is processed.7 PGO waves are associated with increased visual system excitability, arise spontaneously and not via stimulation of the primary visual afferents. Both auditory and somatosensory stimuli influence PGO activity.8 PGO system is also modulated by suprachismatic, amygdaloid, vestibular and brainstem auditory cell groups. The triggering neurons of the pontine PGO wave generator are located within the caudolateral peribrachial and the locus subceruleus areas. The transferring neurons of the pontine PGO generator are located within the cholinergic neurons of the laterodorsal tegmentum and the pedunculopontine tegmentum. The triggering and transferring neurons of the pontine PGO wave generator are modulated by aminergic, cholinergic, nitroxergic, GABA-ergic, and glycinergic cells of the brainstem.9

The most important output structures of those PGO-generating cells are the occipital cortex, entorhinal cortex, piriform cortex, amygdala hippocampus, and many other thalamic, hypothalamic, and brainstem nuclei that participate in the generation of REM sleep. Since PGO-generating cells project to the entorhinal cortex, piriform cortex, amygdala and hippocampus, these PGO-generating cells could also be involved in the modulation of cognitive functions. 10 Recent studies showed that dream also plays a role in the consolidation of memory. 11,12 According to REM-sleep specific neuronal activation dependent consolidation theory, during wakefulness external information makes a temporary impression in the neocortex and the other storage areas of the brain. At the same time this information is processed in specific forms in the amygdala, hippocampus and parahippocampal area. During the REM sleep, with PGO waves the amygdala, hippocampus and parahippocampal area are also activated to organize and consolidate the random information acquired during wakefulness.<sup>13</sup> A theta rhythm (frequency range of 5-10 Hertz) can

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be elicited by both natural sensory stimulation and direct activation of the brainstem reticular formation, can also be elicited from hippocampus throughout REM sleep.<sup>14</sup> Theta frequency waves transfer and bind that consolidated information into the long-term memory storage in the neocortex and other storage areas. 13,15 So REM sleep constitutes a way for hippocampus-driven cortical activation, which may play a role in the communication of memory traces from the hippocampus to the cerebral cortex.16 The processing of dream content which consists of variations in scenarios encountered during daily life in which we interact with the physical and social world is bound to influence our cognitive storage and subsequent appraisal realworld content.<sup>7</sup> The reciprocal interaction between active consciousness and the brain gives opportunity for an interpretation of dreams.<sup>17</sup>

# FUNCTIONAL RELATIONSHIPS BETWEEN THE CORTEX, LIMBIC SYSTEM AND BRAINSTEM IN REM PERIOD

There are functional relationships between amgdale and the cortex during REM sleep. Indeed significantly activated cortical areas (anterior cingulated cortex, parietal operculum) all receive numbers of amgdalar connections. So it was speculated that during REM sleep the diffuse global activation of the cortex by mesopontine reticular formation and thalamus is modulated by the amygdala.<sup>18</sup> Paramedian thalamus is believed to play an important role in the regulation of sleep.<sup>19</sup> However nonspecific structures of the midbrain and the upper parts of the pons, constituting the reticular activating system (RAS), maintain the state of wakefulness. Cells of the locus coeruleus, which contain norepinephrine, serotonin-containing cells of the raphe nuclei, acetylcholine-containing cells of the brain stem and basal forebrain increase their firing rates in anticipation of awakening and during various forms of arousal.<sup>20</sup> They manage the modulation of arousal via ascending cholinergic activation of intralaminar thalamus and descending activation of the subceruleus to generate some of the signs of rapid eye movement sleep. 19 Lesions affecting thalamus and mesencephalic

or pontine tegmental reticular formation are causes of hypersomnia.<sup>21</sup> The amygdala, hippocampus, thalamus, hypothalamus, orbito-frontal cortex and anterior cingulate make up the limbic system which is often referred to as the emotional brain. Amygdala projects directly to cholinergic nuclei in the brainstem that initiate REM state and it triggers the eye movements. Since the amygdaloid complexes are known to associate an affective content to perceptions,<sup>22</sup> it can be speculated that the activation of amygdala and anterior cingulate cortex could account for the emotional aspects of dreaming.<sup>21</sup>

## NEURONAL RELATIONSHIPS CONSTITUTING THE MEMORY OF PEOPLE, EVENTS OR OBJECTS

Neuronal activity-constituted persistent information in the memory-pools, develops an engram between the related neurons. Engram means activity-dependent strengthening of neuronal connections.<sup>23</sup> Memory formation involves different anatomical regions in the brain sets of neuronal circuits and cellular and molecular interactions between and within those neurons. So memories come into being with strengthen synaptic connectivity,<sup>24</sup> by long term potentiation (LTP) mechanism.<sup>25</sup> In other words, a strong relationship is established between the neurons constituting any information rooted in the mind, sometimes addicting on the old information and sometimes newly produced. The more the information is recalled or revived, the stronger this relationship (engram) becomes. Depending on the frequency and/or strength of stimulus, a strengthening of the relationship between the neurons occurs, as the development of new collaterals in the axon terminals of the presynaptic neurons, and as an increase in the synaptic relationship established with other related neurons. An increase in the number of presynaptic axons by LTP related to a postsynaptic neuron, lowers the membrane potential difference -in other words the stimulation threshold- by increasing the excitatory post synaptic potentials (EPSP) of the neuron.<sup>26</sup> Thus, membrane potential is hypo-polarized; the neuron becomes hyper-excitable. This mechanism lowers the stimulation threshold of each neuron coding the same information. These hypo-polarized neurons (in the

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'sub-luminal fringe') may easily create an action potential by a new facilitating stimulus from other relationships.<sup>27</sup> In this way, a neural activation belonging to a different memory, facilitates an action potential in the neural cycle, where this neural activation establishes a random axonal relationship. The axon of each neuron in the central nervous system is divided into thousands of axon branches, on average. These axon terminals establish thousands of synaptic relationships within the related neuronal pool.<sup>28</sup> In our opinion some memory components which are randomly activated by a part of these synaptic relationships may be stimulated simultaneously. Thus the memory neurons related to the people or events and subjects that have dominated recent waking activities are stimulated randomly and independently from the subject integrity, and become the components of a dream scenario. For instance, a person who dreams of her/his grandmother fighting in military uniform with a weapon has probably received effective sensory inputs about some components of this scenario during the day, and she/he has somehow activated the neuronal cycle constituting this information. In other words, she/he has increased the excitability of the neurons of these memories. For example, that person may have been influenced by recently viewing a war scene on TV; by receiving a call from her/his grandmother at the same day. If the neuronal relationships of these recently-stimulated memories establish random synaptic relationships with each other (each neuron is divided into 1000-2000 axon branches, on average, and SSS is believed to include 2 X 10<sup>14</sup> synaptic relationships),<sup>28</sup> it can be concluded that activated neurons can randomly stimulate the neurons of other memories or at least facilitate the stimulation of these neurons. Thus, with the activation of the engrams expressing these unrelated components of the scenario, one can dream absurd scenarios which are based on known objects or sounds.

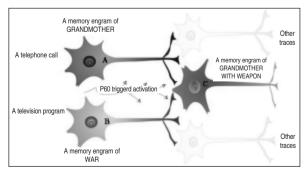
Previous studies show that people who are born blind do not dream visual images; rather, they experience dreams based on audio memory.<sup>29</sup> The implication is that people can not visually dream of an object/person/event which they have never seen before. People only dream of the information obtained in daily life and retained in the brain as a

memory. However, some components of this learned information can combine with components of other information. Such combinations may produce absurd scenarios which are far from the learned information. For instance, a person exposed to the previously-mentioned interactions during the day may potentially dream of a fish holding a weapon in its hand. In this dream, some components of the war scene she/he has watched and of the swimming in the sea have stimulated each other.

We have developed our hypotheses related to the explanation of "probable cell mechanisms of dream scenarios" based on the relationship mechanisms of the neural networks and the long-term potentiation (LTP) mechanisms enabling learning in the hippocampus. The mechanism can be explained via Ganong's "hypothetical nerve net" diagram<sup>27</sup> mentioned random relationships of the neuronal axons (Figure 1).

In figure 1, each of the neurons belonge "Memory A" uses some of its branches of axon (each axon has approximately 1000 branches) to form synapses to neurons C and some other neurons in the neuronal pool. So as a part of these synapses have been developing a functional path (tractus; the ghost neurons in the figure); some branches belonging to "Memory A" may establish random relationships with neurons, for example with C.

Meanwhile, neuron group B -which belongs to another memory- may also establish some random relationships with C. When A and B neuron groups of memories of 2 different events are stimulated simultaneously by the random neuronal activity of



**FIGURE 1:** A neuronal net in the memory storage area. Excitability of a neurons incrased due to a telephone call. Excitability of B neurons incrased by watching television. Components of memories A and B created the dream scenario.

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PGO spikes, the C neurons may also be activated by facilitation, because of the convergens of the A and B neurons on them. Thus, activation initiates a combination of memory pieces represented by A, B and C neuronal groups. As a result; random stimulation of the neurons - constituting components of different memories - by one another can combine to form an absurd dream scenario (Figure 1). This hypothesis on the producing of dream scenarios has been developed based on observations and analysis of the dreams and based on Ganong's "hypothetical nerve net" hypothesis, developed in the scope of summation and facilitation in synaptic transmission.<sup>27</sup>

There are too many studies implying that dream scenarios appear by the random relationships between the neurons of memories; but there is no definitely described mechanism. Crick and Mitchison proposed a 'neural network and REM sleep' theory in 1980s. They asserted that, 'if the stored memories share common features, random stimulation often produces mixed outputs'. This hypothesis may support our idea that, the random connections between the neurons of memories can easily be activated due to daily exitability of the neurons, and may constitute the dream scenario of that day.

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