

## Understanding dreams -the comprehensive, interdisciplinary way: A review

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### Abstract

Dreams are virtual repetitions during sleep, of what we perceive and act, in reality, when we are awake. The basis of wakeful state, is due to the sensory inputs from the sensory organs (through the ascending tracts) and the motor output from the respective brain centres (through the descending tracts), as well as, due to the activated ascending reticular activating system (ARAS) and the posterior hypothalamus. In the dream state, both these sensory inputs and motor outputs are suspended and the ARAS is deactivated. Even the brain's electrical networks i.e the Salience and the Default network, (DMN) are different, during working and sleeping States, respectively. Yet one can see the images of persons and places etc, in the dreams. It follows, that the dreams could be, the unconscious recollection and replay of the past experiences during the sleep. Thus, the dreams are linked to the memory formation, consolidation and its retrieval. Truly, the parts of the brain involved in dreams, are the same as those involved in the consolidation, storage and retrieval of the memory, (Hippocampus) and emotions (Amygdala) and the attempted meaningful interpretation, in the form of a storyline, by the higher brain centers, in the neocortex (like medial prefrontal cortex, etc). In fact, the hippocampus has been shown to utilize the memory, to construct novel, imagined scenarios and simulate possible future events. An area, just above the nape of neck called the "posterior cortical hot zone", is considered to be the "factory of dreams ". The electrical waves (like the Hippocampal theta waves and pontine -geniculate -occipital waves) and the neurotransmitters, (like cholinergic, glutamatergic, adrenergic, serotonergic and GABAergic) link the respective centres involved in the dream process. Several theories (like Freud's, Carl Jung's, activation- synthesis theory etc), are put forward, as well as, several approaches (like Psychodynamic, behavioral and Neuroscience approaches) are followed. The multiplicity of, the theories and approaches, is a testimony to the fact that none of them, has the whole truth. A comprehensive interdisciplinary approach is attempted in this article, by reviewing the various facets of the dreams, like the neuroanatomy of the structures involved, their interconnections, the electro -physiology of the brain, the physiological changes that occur during REM sleep (during which the dreams occur), the clinical entities that mimic the dream- state but are distinct, like, Imagination, Imagery, Recall and the Hallucinations, including, the sleep hallucinations (hypnagogic and Hypnopompic), forebrain Analysis and the forebrain synthesis etc, and sleep disorders (like sleep paralysis, sleep myoclonus) etc., in search of clues, for the better understanding of the subject of dreams.

**Keywords:** Limbic system; Brain electrical waves; REM sleep; Neurotransmitters; Lucid dreams; Consciousness, memory

### 1. Introduction

Dream is a succession of images, ideas, emotions, and sensations witnessed by the mind, during the REM stage of sleep. One of the neuroscience's unsolved mysteries is, why and how the brain dreams. A total of, around two hours is spent, per night, whether they remember it upon waking or not. They are like a movie, produced, directed and screen played by the brain /Mind, the dreamer, being the sole spectator. The dreams are considered, prophetic by the ancient Greeks and Romans, considered meaningless by some scientists, while others opined that dreams improve memory and

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learning, Process emotion, and express our deepest desires. Dreams are considered to have some evolutionary value, training the organism, for the better defence, when awake, and when a potential danger is anticipated [1]. Yet another view is that, the dreams are "garbage generated during information processing and consolidation of the memory, that occurs during REM stage of sleep". Dreams obey, the Circadian rhythm, (cycles that last for 24 hours like, the sleep-wake cycles) and Ultradian rhythms (cycles that repeat in less than 24 hours [2], each cycle lasting for about 90 minutes) consisting of, both REM and NREM stages of the sleep. The advances made in investigative neuroscience, like MRI, EEG, PET scan and polysomnography, etc, have given new insights into the understanding of the dream physiology, leading to enunciation of better physiological theories, compared to the earlier psychological theories. Dreams are like "seeing without seeing".

**Table 1** Facts about dreams

1	Dreams occur 2 hours per night, for 6 years during once life time, each lasting for 5 to 20 minutes.
2	95% of the dreams are forgotten on waking up [3].
3	Less than 10% of dreams are truly bizarre, unrealistic, or fantastic and 80 % are related to daily life activities [4].
4	Animals and birds too dream as evidenced by the REM and NON REM patterns of sleep [5].
5	The born- blind can witness the imagery in dreams as evidenced by the of their eye movements correlated to visual dream recall.
6	External stimuli in using good and bad smells Play a role in positive and negative dreams [6].
7	Higher, the white matter density, greater is the dream recall [7].
8	A 1940 study found that less than 10% get dreams in colours.
9	Lucid dreams, are dreams over which some voluntary control could be exerted, are difficult to be recalled and usually occur during NREM sleep.
10	Dreams like being chased, falling from heights and appearing naked before the society are universal ie. They are dreamt all over the world irrespective of caste, creed, and race.

**Table 2** Theories on dreams

Supernatural theory
Freud Theory
Carl Jung theory
Activation-Synthesis theory
Threat Simulation Theory
Rosalind Cartwright theory
Self organization theory
Expectation fulfillment theory.
Defensive activation theory
Stimulus response theory
Continuation hypothesis
Garbage dump theory of Circk.

In other words, when awake, we see the images in the surrounding with our eyes. But certain images are also seen as in the dreams, when we are not awake (ie, during sleep). Even the born-blind can dream, as could be inferred from the rapid eye movements recorded, while they are asleep. There are other entities, different and distinct from dreams like,

imagination, imagery and recall, and the hallucinations, where mental viewing of images, is possible. The inevitable conclusion of the above findings is, that the sensory stimulus from the five sense organs, is not essential for creating the mental images, and stimulation of any point on their pathway to the brain, is enough to reproduce such an effect. This stimulation is caused by the electrical brain waves, like the theta waves and PGO waves and various excitatory and inhibitory neurotransmitters, during the dreaming. Some of the facts about dreams are presented in the table 1 and the theories are summarized in table 2, as the space precludes a more elaborately consideration of each of them.

## 2. Discussion

The major approaches to dreams, as presented in table 3, each looks at particular facet of the dream. This article reviews the details from an comprehensive interdisciplinary approach of the aspects, enlisted in Table 4, with a view to search clues that might help dreams, understand better.

**Table 3** Major approaches to dreams

Psychodynamic approach
Humanistic approach
Behavioral approach
Cognitive approach
Neuroscience approach

**Table 4** Components of the integrated approach mooted

Insights from the electrophysiology of the brain waves
Insights from the study of Neuroanatomy, including the structures, their interconnections and circuits.
Insights from the Physiological changes observed during the REM sleep.
Insights from the study of the neurotransmitters, in modulating the function of the brain parts.
Insights gained from study of sleep disorders.
Insights gained from the study of Lucid dreams.

### 2.1. Insights from the studies of Electrophysiological changes during REM type of sleep

The types and stages of sleep, their characteristics of a particular stage and the type of associated brain waves as detected by EEG are presented in table 5, below. REM typically lasts 10 minutes to begin with, later REM stages get longer, and finally last up to an hour. It is characterized by an abundance of the neurotransmitter acetylcholine, with a complete absence of monoamine neurotransmitters histamine, serotonin, norepinephrine [8].

Sleep cycle: Alternative NREM and REM cycles operate throughout night.

REM cycles lengthen as night proceeds.

NREM stage 1 – stage 2 – stage 3 – REM

Reverse steps when transition occurs from REM to NREM.

**Table 5** Types of sleep, stages and their characteristics and EEG features of the stage

Type and stage of Sleep	Characteristics of the stage	EEG features of the Brain waves
1.NREM Stage 1	Transition from waking stage to sleeping stage. Easily arousable. Denies of sleeping, if questioned	Alpha waves, which are relatively low frequency (8–13Hz), high amplitude patterns of electrical activity (waves) that become synchronized.
Stage 2	Asleep, but not deeply asleep. Heart and Respiratory rates start a downward trend. Pupils oscillates in diameter.	1. sleep spindles ( a rapid burst of higher frequency brain waves. important for learning and memory.. 2. K-complex is a very high amplitude pattern of brain activity occur in response to environmental stimuli.
Stage 3	Deep sleep. HR and RR decrease. Difficult to arouse. Dreams are difficult to recollect	Delta brainwaves (1-3 Hz) are the slowest, highest amplitude brain waves.
2. REM Stage	Transition from deep sleep to wakeful state. HR and RR increased. Pupils are constricted. Skeletal muscle atony and things of muscles seen. Rapid eye movements are recorded. It is major dreaming stage. Dream content can be recalled	Theta waves are even lower frequency (4–7 Hz), higher amplitude brain waves than alpha waves.

NB: The present classification of NREM staging recognizes only three stages, instead of the earlier 4 stages and hence REM is the 4th stage of sleep.

## 2.2. Ponto-genicul-occipital waves

Ponto-genicul-occipital waves (PGO) are propagating, phasic, field potentials, [9]. between the pons, lateral geniculate nucleus, and occipital lobe. They are generated in a collection of neurons located in the pons [10] especially in the caudolateral peribrachial area. (in cats) They spread toward the lateral geniculate nucleus and the occipital lobe. These are recorded during and immediately before REM sleep [11]. The PGO waves, like epileptiform burstst, spread throughout the brain, potentially via top-down activation by the Amygdala and the Prefrontal Cortex. These potentials also activate the III, IV, and VI cranial nerve nuclei, that cause the rapid eye movements of the REM sleep. Certain limbic structures like Hippocampus (memory) and Amygdala, (related to emotion) are activated by these potentials, Showing that PGO waves generate mnemonic and emotional components of dreams."The pontine nuclei receive inhibitory serotonergic projections from the Raphe nuclei. These mediate the pharmacological links between Serotonin and PGO waves. Thus, Fenclonine and Reserpine that deplete synaptic 5-HT increase PGO wave amplitude. Similarly, 5-HT-1A agonists, suppress PGO wave activity, but not 5-HT-2A agonists" [12]. PGO waves are implicated in the Activation synthesis theory, lucid dreams, active imagination and hallucination [13].

## 2.3. Hippocampal theta rhythm

It has been linked to learning and spatial orientation [14], memory formation [15,16], and navigation [17]. Hippocampal Theta wave activity is seen during REM sleep [18]. Humans also exhibit predominantly cortical theta wave activity during REM sleep [19]. Meditation has been shown to increase theta power [20]. Increased sleepiness is associated with decreased alpha wave power and increased theta wave power [21].

### 2.3.1. Default Mode Network (DMN)

(DMN) or Resting State Network, which includes the medial prefrontal cortex, posterior cingulate cortex, precuneus, hippocampal formation, Parahippocampal cortex, retrosplenial cortex, posterior inferior parietal, temporo- parietal junction, and lateral temporal cortex, with the anterior medial prefrontal cortex and posterior cingulate cortex as the hubs, is the neural network for background consciousness, when the mind is in the state of passive internal mentation, not performing cognitively demanding tasks, and not concentrating on outside stimuli such as when dreaming. Default mode network (DMN), is a highly interconnected in the brain, and is active during sleep, activity in the DMN is strongly associated with stimulus-independent thought, which is also a central feature of dreams. F, Elimination of dreams is correlated with lesions in the ventromedial prefrontal cortex (vmPFC) and the temporo-occipital junction of DMN. The

vmPFC is concerned with motivation, giving weightage to the idea that dreams arise from wishful impulses and other emotional motivations.

**Table 6** Anatomical structures involved in dreams

1. The limbic system	2. Hippocampal complex		3. The basal forebrain structure
Limbic System	A.Hippocampal formation	B Parahippocampal gyrus	Nucleus accumbens Nucleus Basalis
Hypothalamu	Dentate gyrus	Entorhinal Cortex	Diagonal Band of Broch.
Thalamus Hippocampus	Subiculum	Perirrhynal Cortex.	Substantia innoninatim.
Amygdala		Para Hippocampal gyrus.	Medial septal nucleus.

## 2.4. Structures of the Limbic system

### 2.4.1. Hypothalamus

suprachiasmatic nucleus (SCN) sets the circadian rhythm, which controls the sleep - wake cycle. it projects on to the pineal gland to release melatonin, which promotes sleep. The nucleus is synchronized by external cues known as zeitgebers, of which the strongest is the light.

### 2.4.2. Supra mammillary nucleus

Tonic brain stem input is converted into rhythmic firing. They They act as a relay for impulses coming from the amygdalae and hippocampi, via the mamillo-thalamic tract to the thalamus.

## 2.5. Thalamus

### 2.5.1. Anterior nucleus of Thalamus (ANT)

It is a key component of the hippocampal system for episodic memory [22]. The anterior nuclei receive afferents from the mammillary bodies via the mammillothalamic tract and from the subiculum via the fornix. Intern, they project to the cingulate gyrus [23].

### 2.5.2. Lateral geniculate nucleus (LGN)

The LGN, receives information directly from the ascending retinal ganglion cells via the optic tract and from the reticular activating system. Neurons of the LGN send their axons through the optic radiation, a direct pathway to the primary visual cortex. In addition, the LGN receives many strong feedback connections from the primary visual cortex. It is in the pathway of PGO waves. The dentate nucleus regulates fine-control of voluntary movements, cognition, language, and sensory functions.

## 2.6. Hippocampus

### 2.6.1. Functions

Learning, memory, aggression, rage, hormone regulation.

### 2.6.2. Connections

Afferent Pathways: to Entorhinal cortex, septal area, prefrontal cortex, anterior cingulate gyrus, PR mammillary region, reticular formation.

Efferent pathways: septal area (PR commissural fornix), anterior thalamic nucleus, hypothalamic mammillary bodies (post commissural fornix), entorhinal cortex, cingulate cortex, prefrontal cortex, contralateral hippocampus.

## 2.7. The Amygdala

The inputs are from all senses and viscera. Amygdala being important in emotional learning, visceral inputs are a major input source. Visceral inputs come from the hypothalamus, septal area, orbital cortex, and Para brachial nucleus. Olfactory sensory information comes from the olfactory bulb. Auditory, visual and somatosensory information comes from the temporal and anterior cingulate cortices. Major Output Pathways of the Amygdala are Stria terminals, Hippocampus, Entorhinal cortex, Hypothalamus,..septal nuclei.

Through the Ventral Amygdalofugal pathway, It Connects directly to the orectal nucleus of the thalamus. This pathway continues to the anterior olfactory nucleus, anterior perforated substance, piriform cortex, orbitofrontal cortex, anterior cingulate cortex, and ventral striatum. The ventral striatum includes part of the caudate, putamen, and the nucleus accumbens septi. Projections from the ventral striatum are links in a basal ganglia circuit that are important in stimulus-response associative learning [24].

## 2.8. Hippocampal Cortex

### 2.8.1. Dentate nucleus

The dentate nucleus is the cluster of neuron in the cerebellum. Efferent fibers of the dentate nucleus are involved in conscious thought and visuospatial function. The dorsal parts of the dentate nucleus project to the primary motor and premotor areas of the cerebral cortex, while the ventral parts of the dentate project to prefrontal and posterior parietal areas of the cerebral cortex [25]. The dentate nucleus regulates fine-control of voluntary movements, cognition, language, and sensory functions.

### 2.9. Subiculum

Positioned between the hippocampus proper and entorhinal and other cortices, as well as a range of subcortical structures, it mediates the hippocampal - cortex interactions. Input is received from CA1 and layer III pyramidal neurons of EC. It is the main output of the hippocampus. The pyramidal neurons send projections to the nucleus acubens, septal nuclei, prefrontal cortex, lateral hypothalamus, nucleus reunions, mammillary nuclei, entorhinal cortex and amygdala.

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## 3. Parahypocampal structures

### 3.1. The Entorhinal Cortex

The EC is the main interface between the hippocampus and neocortex located in the medial temporal lobe. The entorhinal cortex is the gateway for information entering and leaving the hippocampal formation. Its functions relate to memory, navigation, and the perception of time. The superficial layers – layers II and III – of EC project to the dentate gyrus and hippocampus: Layer II projects primarily to dentate gyrus and hippocampal region CA3; layer III projects primarily to hippocampal region CA1 and the subiculum. These layers receive input from other cortical areas, especially associational, perirhinal, and Para hippocampal cortices, as well as prefrontal cortex.

### 3.2. The perirhinal cortex

The perirhinal cortex is involved in both visual perception and memory; it facilitates the recognition and identification of environmental stimuli. The perirhinal cortex is involved in both visual perception and memory; it facilitates the recognition and identification of environmental stimuli. It interconnects the hippocampal formation together with other parts of the limbic lobe and with the lateral temporal and occipitotemporal association cortices. essential to memory formation and high level visual processing.

### 3.3. Para Hippocampal gyrus

It surrounds the hippocampus and plays an important role in both spatial memory and navigation. PPA represents scenes in a viewpoint-specific manner (Epstein, R. et al., 2003) and processes the spatial structure of the currently visible environment (Epstein, R. et al., 1999).

### 3.4. Para hippocampal cortex (PHC)

It plays a key role, in episodic memory, spatial processing, and the encoding of novel stimuli and contextual associative processing.

### 3.5. The basal fore brain structures

These are located in the forebrain to the front of and below the striatum. They include Nucleus acumens Nucleus basalis, Diagonal Band of Broca, substantia innominata, Medial septal nucleus.

### 3.6. Nucleus Acubens

It is concerned with slow wave sleep, Reward-Reinforcement, aversion and addiction, functions. The Inputs are the glutamatergic projections from PFC, Hippocampus; Amygdala, Dopaminergic projections from VTAcetylcholinergic projections from the tuber mammillary nucleus (the sole source of histamine neurons in the brain). The outputs are to nucleus acubens - the basal ganglia and the ventral pallidum (VP). the medial dorsal nucleus of the dorsal thalamus, prefrontal cortex as well as back to the ventral and to dorsal striatum. Diagonal band of Broca is believed to be involved in the generation of theta waves in the hippocampus [26]. It also inhibits magnocellular neurosecretory cells via GABA interneurons [27].

#### 3.6.1. Nucleus basalis of Meynert or nucleus basalis magnocellularis

It is a group of neurons located mainly in the substantia innominata of the basal forebrain [28]. These neurons are rich in acetylcholine. These cells are associated with arousing stimuli, both positive (appetitive) and negative (aversive) sustained attention [29], learning and recall in long term memory. It is to modulate the ratio of reality and virtual reality components of visual perception [30].

### 3.7. Diagonal band of Brock

Diagonal band of Broca, is believed to be involved in the generation of theta waves in the hippocampus [31]. It also inhibits magnocellular neurosecretory cells via GABA interneurons [32]. The subcallosal gyrus in the septal area with the hippocampus and lateral olfactory area. This is a cholinergic bundle of nerve fibers posterior to the anterior perforated substance. It interconnects the subcallosal gyrus in the septal area with the hippocampus and lateral olfactory area. Two structures make up the DBB namely the nuclei of the vertical and horizontal limbs of the diagonal band of Broca (MS/DB and nhlDBB, respectively). nvlDBB projects to the hippocampal formation through the fornix and it is the second largest assembly of cholinergic neurons in the basal forebrain whereas nhlDBB projects to the olfactory bulb and it does not have a significant population of cholinergic neurons [33].

### 3.8. The medial septal nucleus

This part of basal forebrain supports many physiological functions, from sensorimotor integration to cognition. A major projection from the medial septal nucleus terminates in the hippocampal formation. The septal nuclei receive reciprocal connections from the olfactory bulb, hippocampus, amygdala, hypothalamus, midbrain, habenula, cingulate gyrus, and thalamus. The septal nuclei are essential in generating the theta rhythm of the hippocampus [35].

### 3.9. Brain stem

It is responsible for many vital functions of life, such as breathing, consciousness, blood pressure, heart rate, and sleep. Ascending Reticular Activating System (ARAS), functions to arouse the cerebral cortex, to awaken the brain to a conscious level, and to prepare the cortex to receive the rostrally projecting impulses from any sensory modality. The changes in heart and respiration with each stage of sleep is an evidence that the sleep centre's are coupled to respective brainstem nuclei. Neurotransmitters are produced in all of these areas and sent throughout the central nervous system to modulate sensory perception, motor activity, and behavioral responses. The important areas of ARAS.

**Table 7** Important areas of brainstem and the neurotransmitter secreted by each

Area of brainstem	Type of neurons	Neurotransmitter transmitter secreted
Ventral tegmental area.	Dopaminergic.	Dopamine
Locus ceruleus	Noradrenergic	Noradrenaline
Raphe nucleus.	Serotonergic	Serotonin
Anterodorsal tegmental Nucleus	Cholinergic	Acetylcholine

#### 4. Insights from the Physiological changes that occur during REM sleep:

Certain physiological changes occur during REM sleep and their cause-effect relation to dreams that occur during the same period are worthy of investigation.

The physiological changes occurring in REM sleep are being summarized in table 8 below. A brief consideration is given to the conditions mentioned there in.

**Table 8** Physiological changes during REM sleep

Rapid eye movements.
Increased Heart rate
Increased rate of breathing.
Contractions of extraocular muscles.
Skeletal muscle atonia.
Penile erections in males
Clitoral enlargement in females
Pupillary constriction.
Cessation of thermoregulation
Contraction of middle ear muscles.
Presence of pontine-geniculate-occipital (PGO) waves as well as hippocampal theta EEG activity
Memory consolidation and replenishment of depleted chemicals, such as serotonin.
Twitching of muscles of face and limbs.
Increase regional blood supply to brain, increased glucose uptake, by brain cells with relatively less uptake of the oxygen.

##### 4.1. Insights from the Physiological changes that occur during REM sleep

The physiological changes occurring in REM sleep are being summarized in table 7. A brief consideration is given to the conditions mentioned there in.

##### 4.2. Rapid Eye movements

Electrical and chemical activity regulating this phase seems to originate in the brainstem, and is characterized most notably by an abundance of the neurotransmitter acetylcholine, combined with a nearly complete absence of monoamine neurotransmitters, histamine, serotonin and norepinephrine. This is coupled to muscular atonia. In Rapid eye movements behaviour disorder, the atony is inhibited resting in undesirable motor activity like shouting and kicking etc resulting in injuries to self or bed-mates.

##### 4.3. Changes in heart rate (HR) and respiratory rate (RR)

During the NREM sleep, alpha wave activity and cardiac rate correlates showed opposite variations, with high levels of alpha power associated with decreased heart rate, rRR and LF/HF ratio, indicating low sympathetic activity. Conversely, during REM sleep, alpha activity was low whereas heart rate, rRR, and the LF/HF ratio peaked, indicating high sympathetic activity. There is a correlation between LF (low frequency waves) and HF (high frequency waves). The ratio of LF to HF reflects the sympathovagal balance. An increased LF/HF ratio indicates low vagal activation. In healthy subjects, LF and HF have a circadian pattern with reciprocal fluctuations. In the daytime LF increases, in the night time HF increases. LF increases during 90-degree tilt, mental stress, standing, occlusion of coronary arteries, moderate exercise, and occlusion of carotid arteries. HF increases in cases of respiration, cold application on the face and rotational stimulation [35]. L6w Frequency (LF): includes the frequency range between 0.04 Hz and 0.15 Hz and is

co].nsisting of a combination of sympathetic and parasympathetic effects [36]. It is associated with thermoregulation and peripheral vasomotor activity. The recording time is short-term (1-5 min) and long-term (entire 24 hours [37].

High Frequency (HF): (frequency range between 0.16 Hz and 0.4 Hz.) is modulated by the parasympathetic activity of ANS and that is the major determinant of respiratory sinus arrhythmia.

#### **4.4. pupil size**

During the awake state, the pupil remains dilated most of the time. During REM sleep, it remains mostly constricted, whereas during NREM sleep, the pupil's diameter continually oscillates between small and large blocking the parasympathetic drive by tropicamide application dilated the pupil and removed its prominent fluctuations during NREM sleep. More importantly, tropicamide treatment abolished the coupling that existed between pupil size and cortical activity. These results suggest that fluctuations in pupil diameter during sleep are mainly driven by the parasympathetic pathway [38]. Variations in pupil size can predict arousal, vigilance levels and emotional responses. [39]

#### **4.5. Muscle atonia of REM sleep**

It occurs as a result of inhibition of motor neurons in the spinal cord by release of inhibitory neurotransmitters and glycine and gamma-aminobutyric acid, and to disaffiliation due to removal of brainstem excitatory inputs to motor neurons that are normally present during waking and nonrapid sleep. During REM sleep, skeletal muscles are paralyzed in one moment but twitch and jerk in the next.

##### *4.5.1. REM sleep twitches*

These are traditionally considered random motor events that result from momentary lapses in REM sleep paralysis. Twitches are not byproducts of REM sleep, but are in fact self-generated events that could function to promote motor learning and development. GABA and glycine drive on to motoneurons prevents twitch activity during REM initiation, but progressive weakening of this drive functions to promote twitch activity during REM termination.

#### **4.6. sexual stimulation in REM sleep**

During the REM stage in sleep, the blood flow in the pelvic region gets boosted. This leads to erection in men and vaginal wetting in women. Absence of norepinephrine, which prevents blood flow to the genitalia and also prevents erections, is inhibited, during REM. Sleep. Sexual dreams are not considered a type of sexsomnia because they do not involve physical actions or behaviours aside from arousal and ejaculation.

##### *4.6.1. Sexsomnia episodes*

They occur mostly during non-rapid-eye-movement (NREM), the dreamless, deepest stage of the sleep cycle. This is a parasomnia, in which the person indulges in sleep sex, about which he is not aware of when woke up, next morning, during

#### **4.7. Thermoregulation in REM sleep**

Metabolism can drop by 10 percent in sleeping people. Thermogenesis is strongly coupled to REM sleep but how it affects dreaming is not clear. There is a slight increase in body temperature in REM sleep. This is due to increased blood flow due to vasodilatation of Carotid artery and more so in vertebral arteries and peripheral vasodilatation. This is independent of Circadian rhythm control of thermogenesis.

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### **5. The haemodynamic and metabolic changes during dream state/REM stage of sleep**

These are discussed under the heading, summary, below

#### **5.1. Insights from seemingly related but distinct conditions**

##### *5.1.1. Imagination*

Imagination is the ability to produce and simulate novel objects, sensations, and ideas in the mind without any immediate input from the senses. It is also described as the forming of experiences in one's mind, which can be recreations of past experiences, such as vivid memories with imagined changes, or completely invented and possibly fantastic scenes [40]. There are two types, the reproductive or Imagery and Productive or "constructive" imagination.

The constructive imagination is further divided into voluntary imagination driven by the lateral prefrontal cortex (LPFC) and involuntary imagination (LPFC-independent), such as REM-sleep dreaming, daydreaming, hallucinations, and spontaneous insight [41]. The voluntary types of imagination include integration of modifiers, and mental rotation. Imagined images, both novel and recalled, are seen with the "mind's eye".

#### 5.1.2. *Imagery*

"Mental imagery" denotes, in psychology the process of reviving in the mind, recollections of objects that evoked sense perception previously, such as details of taste, touch, sight, smell, and sound. In addition, movement or sense, of a body in motion (kinesthetic imagery) or the emotions of a person, such as fear or hunger (organic imagery or subjective imagery) also forms a part of imagery.

Imagination is the ability to form a mental image of something that is not perceived through the five senses. It is the ability of the mind to build mental scenes, objects or events that do not exist, are not present, or have happened in the past. It is the production of mental images associated with previous percepts, and imagination as the faculty of forming mental images of a novel character, relating to something, that has never been actually experienced by the subject but at a great extent emerges from his inner world.

**Recall**, in psychology, the act of retrieving information or events from the past while lacking a specific cue to help in retrieving the information. A person employs recall, for example, when reminiscing about a vacation or reciting a poem after hearing its title.

### 5.2. Prefrontal Analysis (PFA)

It is a type of active constructive imagination that allows humans to mentally reduce an object into parts. Desynchronization of the part of an object-encoding neuronal ensemble (objectNE) from the rest of the ensemble. For example, when one imagines a kettle with a broken handle, the lateral prefrontal cortex (LPFC) desynchronizes the handle from the rest of the object NE of the kettle. LPFC-driven shift of a part of the objectNE out-of-phase with the rest of the ensemble, results in the perception of a new object encoded by those neurons that remain firing synchronously.

### 5.3. Prefrontal Synthesis (PFS)

It is the conscious, purposeful, process of synthesizing novel mental images. PFS is neurologically different from the other types of imagination, such as simple memory recall and dreaming. Unlike dreaming, which is spontaneous and not controlled by the prefrontal cortex (PFC) [42]. PFS is controlled by and completely dependent on the intact lateral prefrontal cortex [43]. Unlike simple memory recall that involves activation of a single neuronal ensemble (NE) encoded at some point in the past, PFS involves active combination of two or more object-encoding neuronal ensembles (object NE). The mechanism of PFS is hypothesized to involve synchronization of several independent object NEs.

### 5.4. Hallucinations

These are similar experiences to that of dreams, as far as viewing mental pictures of things, but, a with difference. "Hallucinations are "perception-like experiences that occur without an external stimulus. "These perceptions are vivid and seem very real. As against dreams, they occur in wakeful state and has pathological background of the brain. They lie outside the voluntary control of the person experiencing them and neither relate to the five sensory perceptions.

### 5.5. Sleep Hallucinations

There are two forms of sleep related hallucinations are called

- Hypnagogic hallucinations (Hypnagogia)
- Hypnopompic hallucinations. (hypnopompia).

Hypnagogic hallucinations occur during transition from wakeful to sleep state, and may be accompanied by sleep paralysis, a state in which the subject is physically immobile but fully conscious.

Hypnopompic hallucinations, occurs during transition from asleep to wakeful state. Hypnopompia, which is often considered as part of a dream by the subject, also involves difficulty breathing and muscle tightness.

## 5.6. Insights from Sleep disorders

A thin line separates, the physiological disorders from the pathological disorders. sleep disorders are one such group of pathological disorders which are just an extension of physiological entities. So these pathological extensions offer insights into the physiology counterparts.

- During REM sleep there is muscular atony /paralysis which recovers on waking up. In Sleep paralysis, the paralysis during sleep continues even on waking up.
- Muscle Twitching occurring during REM- sleep are physiological, but if sustained and repetitive leads to "Sleep myoclonus "which is pathological.

## 5.7. Insights from the Lucid dreams

lucid dream is a type of dream, where the dreamer, may gain some amount of control over the dream characters, narrative, or environment. They occur during NREM sleep, where as, in vivid dreams of REM sleep, the dreamer is unaware of the content of the dream and is completely involuntary. Perhaps the difference is due to the electrical activity during NREM, delta waves, being predominant whereas during REM sleep, the theta waves prevail. Further, the PFC is switched off during REM sleep, while it is switched on during NREM sleep. This makes, all the difference in " self awareness", which is a function of PFC.

## 5.8. Summary

- Dreams arise by interaction of anatomical structures, constituting the Limbic system, hippocampal complex and basal forebrain.
- The ascending reticular activating system, (ARAS) concerned with the arousal of the organism, keeps the arousal low during sleep. Some of the higher brain centres like PFA etc., concerned with cognition and Self awareness, are switched off in REM stage of sleep. The keeping alert of the occipital visual cortex, through stimulation by the PGO waves and the auditory cortex, by impulses arising from the contractions of the middle ear muscles during REM sleep alert even during sleep, could have some evolutionary importance concerned with defense of the individual, should, a threat arise during sleep. For example, a small sound during sleep, will wake up the sleeping individual.

### On and Off switches in the brain :

- Ahmed A. Moustafa et al (2015) in their article titled " on and off switches of brain" reviewed this aspect [44]. Melanin-containing neurons and Orexin ( also known as hypocretin, is a neuropeptide that regulates arousal, wakefulness, and appetite) neurons, which act as Off and On switches for regulating respectively, are in the lateral hypothalamus which regulate sleep (Hassani et al. 2009) [45]. Orexin overexpression is related to insomnia (Prober et al., 2006) [46]. and that Orexin deficiency is related to narcolepsy (Chemelli et al ) [47].
- On and off switches for motor activity correspond to dopamine D1 and D2 neurons in the striatum. Also, the lateral prefrontal cortical regions have off motor switches (Sakagami et al., 2001) [48].
- For fear response, the intercalated neurons send inhibitory, while the fear-expression basolateral neurons, send excitatory, projections to the central nucleus of the amygdala, which initiate fear responses. Alanine and GABA, can also act as sleep switch, as both are suppressed during sleep (Wulff et al, 2010) [49].This explains why even a small sound wakes up a person suddenly from REM sleep, as the thalamus is active, sending the cortex images, sounds, and other sensations that fill our dreams. dreams. The thalamus switches off connections to the spinal cord, resulting in blocking of sensory and the voluntary motor activities.
- Brainstem nuclei modulate the control of the vital organs like the Heart and lungs,as seen in the NREM and REM stages. The hypothalamus modulate the sleep wake cycle ( Cicardian rhythm) and the autonomic dysregulation, the effects of which are seen in REM stage, when dreams occur. These effects includes pupillary oscillations in NREM sleep, and constricted pupil during REM, sexual stimulation and dysregulation of thermoregulation.

- The physiological activity during rapid eye movement (REM) sleep are directly related to the concurrent dream experiences [50, 51, 52, 53]. The Rapid eye movements, represent scanning responses of the visual dream images. On the otherhand pharmacological suppression of REM sleep, for instance, did not eliminate dreaming (Oudiette et al., 2012) [54] and specific forebrain lesions (Solms, 2000) [55]. were shown to suppress dreaming without affecting REM sleep.
- The role of Adenosine in REM sleep :
- In the transition from NREM to REM sleep, a marked increase in cerebral blood flow and glucose uptake by the brain is observed, together with a lesser increase in O<sub>2</sub> uptake. There is increased splitting of of ATP, resulting in increased production of adenosine. This in turn stimulates sleep. Prolonged neural activity in the brain's arousal centers triggers the release of adenosine, which in turn slows down neural activity in the arousal center areas.
- The resting brain is still under the influence of electrical rhythms, which vary according to the stage of sleep. Thus NREM sleep stage 1 shows, Alfa brain waves, stage 2 shows electrical spindles and K complexes and stage 3 shows delta waves. The REM stage is characterised by theta waves. Low Frequency (LF) includes the frequency range between 0.04 Hz and 0.15 Hz and is consisting of a combination of sympathetic and parasympathetic effect. It is associated with thermoregulation and peripheral vasomotor activity. High Frequency (HF) ( frequency range between 0.16 Hz and 0.4 Hz.), is modulated by the parasympathetic activity of ANS and that is the major determinant of respiratory sinus arrhythmia. The ratio of LF to HF reflects the sympathovagal balance. increased LF/HF ratio indicates low vagal activation A decreased LF/HF indicates high sympathetic activity.
- Physiological activity during rapid eye movement (REM) sleep are directly related to concurrent dream experiences. REMs represent scanning responses of the visual dream images. cross talk between the various aforesaid structures, is facilitated by the rich, connecting neural pathways between them. The generation and transmission of the impulses is to the target areas is through electrical waves like the theta waves and PGO waves and through various neurotransmitters, both excitatory and inhibitory. Various anatomical structures are involved in the production of these neurotransmitters. cholinergic neurons (basal forebrain and pons-midbrain) Dopaminergic neurons (midbrain), glutamate receptors (throughout the brain and spinal cord), GABAergic neurons - (hippocampus, thalamus, basal ganglia, hypothalamus, and brainstem). serotonergic neurons ( raphe nucleus), Histaminergic neurons (tuberomammillary nucleus of the posterior hypothalamus) Hippocampus and Amygdala, are the most important in dream generation, as memory consolidation, storage and retrieval and are coupled to dream process, especially, the declarative memory including the episodic memory is the chief source of the content of the dreams. The emotional content is supplied by Amygdala. Meaningful interpretation of the dream is given by the basal forebrain structures. The response of these neurotransmitters is dependent on the types and subtypes of post- synaptic receptors on which they act. Thus a single neurotransmitter might have opposite effects, for example, acetylcholine is excitatory at neuromuscular junction (nicotine action) but inhibitory to heart muscle (Muscatinic action).
- The electrical and chemical activity regulating REM stage of the sleep, seems to originate in the brain stem, and is characterized most notably by an abundance of the neurotransmitter acetylcholine, combined with a nearly complete absence of monoamine neurotransmitters histamine, serotonin and norepinephrine.[56].
- The brain can not synthesize, de novo, any new objects. The objects, faces and people seen in the dreams are drawn from the information stored as declarative / episodic memory, which is recognized to be processed and consolidated during REM sleep and hence may appear familiar but not strange. The converse is also true, that what has not been experienced before or stored in memory can not be recognised and hence appear strange. The seemingly bizarre incidents dreamed, might arise from the unconnected bits of information rejected during memory consolidation of the events that happened, during the day, or the mistaken attempt of the higher brain centres trying to give a meaningful interpretation of the disjointed information, received from the memory consolidation, from the hippocampus, forebrain synthesis or forebrain analysis may also play a role in the bizarre content of the dreams. The metaphor ' we use in daily life are also thought to be influencing the bizarre dreams, for example, a metaphor used, like " down under the heap " might be literally perceived and projected as if one actually is under a heap, during the dream.
- The sleep disorders, might offer some clues to dreams, which are physiological as a thin line separate the normal / physiological from the abnormal / pathological entities like sleep paralysis and sleep myoclonus, which are extended forms of the physiological muscle atony and muscle twitching, respectively of REM sleep. For example, if one may experience to walk in dream, it is phsiological, but if one really walks in sleep (sleep

walk) it is pathological. The difference is, during dream sleep / (REM) state, the skeletal muscles are paralyzed, due to the synaptic inhibition by GABA, a seemingly defensive mechanism preventing from enacting / reacting to what one dreamt, which might otherwise cause injury to self or others. Imagine what happens, if this synaptic inhibition is prevented. Another sleep disorder is "sleep paralysis" in which the physiological paralysis is sustained, transforming the physiological state to a pathological disease. D1 and D2 dopamine neurons in the striatum have on/off switches for motor activity, as above. Also, the lateral prefrontal cortical regions have off motor switches. The sustained shift of balance in favour of the dopaminergic neurons, may be responsible for hypnic myoclonus. Orexin over expression is related to insomnia and that orexin deficiency is related to narcolepsy (Chemelli et al, 1999)

- Clinical entities resembling but distinct from dreams like imagination, Imagery, Recall and hallucinations too, create mental images, but all of them occur in wakeful state, while dreams operate in the state of sleep. Thus if Consciousness or otherwise are defined the mechanisms that underlie, may be similar, a point that demands researchers attention. Hypnagogic and hypnopompic hallucinations which respectively occur in waking to sleeping and sleeping to waking transition states of sleep. They are in fact similar to dreams but are labelled as hallucinations. Hippocampal damage disrupts dreaming, much in the same way that it also disrupts imagination.
- Thus, these might represent a continuous spectrum, at one end of which are dreams (which occur during sleep state) and the other end are imagination etc (which occur during wakeful stage) with sleep hallucinations, (occurring during the transitional stage), representing the middle of the spectrum. Further, it is known that the theta waves and PGO waves are implicated in the two broad groups, on either end of the spectrum.
- It is suggested that, de-linking the mechanisms underlying the sleep-wake cycle and arousal system, a common mechanism involving the dreams and the aforesaid allied but distinct entities might be possible, a lead that is worth pursuing, in future research.
- The Lucid dreams of NREM differ from the vivid dreams of REM Stage, in that in the former, the person is 'consciously aware' of the dreaming state where as in the later there is no conscious awareness. It is known that the conscious awareness along with the other cognitive qualities are, the function of the basal prefrontal cortex of the brain. The same is switched off in REM stage and switched on in NREM stage, which explains the difference between the two types of dreams. It is also known that the predominant brain wave in NREM and REM stages are the delta and theta waves, respectively, whose frequencies differ. REM sleep, characterized by wake-like, globally 'activated', high-frequency electroencephalographic activity. Dreaming in non-REM NREM sleep, characterized by prominent low-frequency activity. [57] How the effects of low frequency (LF) and high Frequency (HF) waves (HF) elicit different responses with regard to HR and RR, is seen above. Both REM and NREM sleep, dreaming is associated with local decreases in slow wave activity (SWA) in posterior brain regions. [58].

## 6. Conclusion

There is some truth, but not the whole truth, in each of the theories advanced and approaches followed, with respect to the dreams, as evidenced by their multiplicity. The truth is always in the middle, when diverse views are expressed. Thus, it is felt that there is a need for an interdisciplinary integrated approach to understand dreams. The latest investigative advances in neurosciences gave an edge to the physiological as against the earlier psychological theories as the former are evidence based. There are potential advantages in searching for clues, to the alluding problem of dreams, in allied but distinct entities, like imagination, Imagery, recall and hallucinations, which also present mental pictures as do dreams, but in wakeful state. Likewise, the physiological fallouts of dream might also throw some light on dreams, if carefully pursued. So are the, sleep disorders, some of which are the pathological extensions of the physiological events that occur during the dream producing REM stage of the sleep. These issues are focused, to stimulate the possible follow up, in future research.

## References

- [1] Zadra A, Desjardins S, Marcotte E. Evolutionary function of dreams: A test of the threat simulation theory in recurrent dreams. *Conscious Cogn*. 2006 Jun;15(2):450-63.
- [2] Wamsley EJ, Hirota Y, Tucker MA, Smith MR, Antrobus JS. Circadian and ultradian influences on dreaming: a rhythmic. *Brain Research Bulletin*, 71(4), 347–354.

- [3] Dr Gimmaro L, Cipolli C, Cherubini A et al. amygdala and hippocampus volumetric and diffusivity in relation to brain. *Hum Mapp.* 2011; 32 (9) : 1458-70. Manager PR, Siegal JM, Do All mammals dream ? *J.Comp.Neural.* 2020 ; 526 (17): 3198- 3204
- [4] Manager PR, Siegal JM, Do All mammals dream ? *J.Comp.Neural.* 2020 ; 526 (17): 3198- 3204
- [5] Shredl M, Atanasova D, Hofmann K, Maurer JT, Hummel T, Stuck BA. Information processing during sleep.. *sleep Research* 2009;18(3):
- [6] Wallat R, Eichenlaub JB, Nicola, A, Ruby P. Dream recall frequency associated with medial forefront brain cortex white matter density. *Front. Psychol.* 2018 ; 9: 1856.
- [7] Murxyn E, Do we dream in colour? A comparison of the reported colour dreams in the younger and the older adults with different experiences of the black and white media. *conscious.Cogn* 2008; 17(4): 1228 - 3711
- [8] Ritchie E. Brown & Robert W. McCarley (2008), "Neuroanatomical and neurochemical basis of wakefulness and REM sleep systems", in *Neurochemistry of Sleep and Wakefulness* ed. Monti
- [9] Gott, Jarrod A.; Liley, David T. J.; Hobson, J. Allan (2017). "Towards a Functional Understanding of PGO Waves". *Frontiers in Human Neuroscience*. 11: 89..
- [10] Lim, Andrew S.; Lozano, Andres M.; Moro, Elena; Hamani, Clement; Hutchison, William D.; Dostrovsky, Jonathan O.; Lang, Anthony E.; Wennberg, Richard A.; Murray, Brian J. (2007-07-01). *Sleep*. 30 (7): 823-827..
- [11] Datta, S.; Hobson, J.A. (1994). "Neuronal activity in the caudo-lateral peribrachial pons:Relationship to PGO waves and rapid eye movements". *J. Neurophysiol.* 71 (1): 95–109.
- [12] Jarrod A. Gott, David T. J. Liley, and J. Allan Hobson. *Towards a Functional Understanding of PGO Waves*. *Front Hum Neurosci*. 2017; 11: 89.
- [13] Lomas T, Ivitan I, Fu CH "A systematic review of the neurophysiology of mindfulness on EEG oscillations" (PDF). *Neuroscience & Biobehavioral Reviews*. 57: 401–410. (2015).
- [14] Yu AJ, Dayan P (May 2005). "Uncertainty, neuromodulation, and attention". *Neuron*. 46 (4): 682–92.
- [15] Winson, J. (1978-07-14). "Loss of hippocampal theta rhythm results in spatial memory deficit in the rat". *Science*. 201 (4351): 160–163.
- [16] Datta, S.; Hobson, J.A. (1994). "Neuronal activity in the caudo-lateral peribrachial pons:Relationship to PGO waves and rapid eye movements". *J. Neurophysiol.* 71 (1): 95–109.
- [17] Gott, J.A.; Liley, D.T.J.; Hobson, J.A. (2017). "Towards a Functional Understanding of PGO Waves". *Front. Hum. Neurosci*. 11: 89.
- [18] Sealer, Matthew A.; Johnson, Lynn D.; Chabot, Elizabeth S.; Asaka, Yukiko; Berry, Stephen D. (2002-02-05). "Oscillatory brain states and learning: Impact of hippocampal theta-contingent training". *Proceedings of the National Academy of Sciences of the United States of America*. 99 (3): 1616–1620.
- [19] Winson, J. (1978-07-14). "Loss of hippocampal theta rhythm results in spatial memory deficit in the rat". *Science*. 201 (4351): 160–163. Bibcode:1978Sci...201..160W.
- [20] Buzsáki, György; Moser, Edvard I. (2013). "Memory, navigation and theta rhythm in the hippocampal-entorhinal system". *Nature Neuroscience*. 16 (2): 130–138.
- [21] ATN Child, ND; Benarroch, EE (19 November 2013). "Anterior nucleus of the thalamus:functional organization and clinical implications". *Neurology*. 81 (21): 1869–1976.
- [22] Jankowski, Maciej; Ronnqvist, Kim; Tsanov, Marian; Vann, Seralynne; Wright, Nicholas; Erichsen, Johnathan Aggleton, John; O'Mara, Shane (30 August 2013). "The Anterior Thalamus Provides a Subcortical Circuit Supporting Memory and Spatial Navigation". *Frontiers in Systems Neuroscience*. 2013; 7: 45.
- [23] Cudeiro, Javier; Sillito, Adam M. (2006). "Looking back: corticothalamic feedback and early visual processing". *Trends in Neurosciences*. 29 (6): 298–306. CiteSeerX 10.1.1.328.4248.
- [24] Rajmohan V, Mohandas E. The limbic system. *Indian J Psychiatry*. 2007 Apr;49(2):132-
- [25] Dum, R. P., & Strick, P. L.. An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex. [Article]. *Journal of Neurophysiology*, 89(1), 634–639 (2003)

- [26] kemoto S (November 2010). "Brain reward circuitry beyond the mesolimbic dopamine system: a neurobiological theory". *Neuroscience and Biobehavioral Reviews*. 35 (2): 129–50.
- [27] Malenka RC, Nestler EJ, Hyman SE (2009). Sydor A, Brown RY (eds.). *Molecular Neuropharmacology: A Foundation for Clinical Neuroscience* (2nd ed.). New York: McGraw-Hill Medical. pp. 147–148, 367, 376.
- [28] Hedreen JC (1984). "Topography of the magnocellular basal forebrain system in human brain". *Journal of Neuropathology and Experimental Neurology*. 43 (1): 1–21.
- [29] Liu AK; et al. (2015). "Nucleus basalis of Meynert revisited: anatomy, history and differential involvement in Alzheimer's and Parkinson's disease". *Acta Neuropathologica*. 129 (4): 527–540.
- [30] Liu, A. K. L.; Lim, E. J.; Ahmed, I.; Chang, R. C.-C.; Pearce, R. K. B.; Gentleman, S. M. (December 2018). "Review: Revisiting the human cholinergic nucleus of the diagonal band of Broca". *Neuropathology and Applied Neurobiology*. 44 (7): 647–662.
- [31] Brown, Colin H. (2016). "Magnocellular Neurons and Posterior Pituitary Function". *Comprehensive Physiology*. American Cancer Society. 6 (4): 1701–1741.
- [32] Mesulam MM (2013). "Cholinergic circuitry of the human nucleus basalis and its fate in Alzheimer's disease". *Journal of Comparative Neurology*. 521 (18): 4124–44.
- [33] Ritchie E. Brown & Robert W. McCarley (2008), "Neuroanatomical and neurochemical basis of wakefulness and REM sleep systems", in *Neurochemistry of Sleep and Wakefulness*
- [34] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *Eur Heart J* 17: 354–381..
- [35] Kayıkçıoğlu M, Payzın S (2001) Heart Rate Variability. *Arch Turk Soc Cardiol* 29: 238-245.
- [36] Kurtoğlu E, Aktürk E, Korkmaz H, Ataş H, Cuğlan B, et al. (2013) Impaired heart rate variability in patients with mitral annular calcification: An observational study. *Anat Card J* 13: 668-674.
- [37] Singh JP, Larson MG, Tsuji H, Evans JC, O'Donnell CJ, et al. (1998) Reduced heart rate variability and new-onset hypertension: insights into pathogenesis of hypertension: The Framingham Heart Study. *Hypertension* 32: 293–297.
- [38] Özge Yüzge, Mario Prsa, Robert Zimmermann, and Daniel Huber. Pupil Size Coupling to Cortical States Protects the Stability of Deep Sleep via Parasympathetic Modulation. *Curr Biol*. 2018 Feb 5; 28(3): 392–400.
- [39] Partala T., Surakka V. Pupil size variation as an indication of affective processing. *Int. J. Hum. Comput. Stud.* 2003;59:185–198. [Google Scholar]
- [40] Vyshedskiy, Andrey (2020). "Voluntary and Involuntary Imagination: Neurological Mechanisms, Developmental Path, Clinical Implications, and Evolutionary Trajectory". *Evolutionary Studies in Imaginative Culture*. 4 (2): 1–18. doi:10.26613/esic.4.2.186. ISSN 2472-9884.
- [41] Braun, A. (1 July 1997). "Regional cerebral blood flow throughout the sleep-wake cycle. An <sup>1</sup>H<sub>2</sub>(15)O PET study". *Brain*. 120 (7): 1173–1197. doi:10.1093/brain/120.7.1173. PMID 9236630.
- [42] Christoff, Kalina; Gabrieli, John D. E. (4 November 2013). "The frontopolar cortex and human cognition: Evidence for a rostrocaudal hierarchical organization within the human prefrontal cortex". *Psychobiology*. 28 (2): 168–186.
- [43] Ahmed A. Moustafa. On and Off switches in the brain. *Front. Behav. Neurosci.*, 29 April 2015.
- [44] Oum Kaltoum Hassani, Maan Gee Lee, Pablo Henny and Barbara E. Jones
- [45] Discharge Profiles of Identified GABAergic in Comparison to Cholinergic and Putative Glutamatergic Basal Forebrain Neurons across the Sleep-Wake Cycle *Journal of Neuroscience* 23 September 2009, 29 (38) 11828–11840.
- [46] David A. Prober, Jason Rihel, Anthony A. Onah, Rou-Jia Sung and Alexander F. Schier Hypocretin/Orexin Overexpression Induces An Insomnia-Like Phenotype in Zebrafish *Journal of Neuroscience* 20 December 2006, 26(51): 13400-13410.

- [47] Chemelli RM, Willie JT, Sinton CM, Elmquist JK, Scammell T, Lee C, Richardson JA, Williams SC, Xiong Y, Kisanuki Y, Fitch TE, Nakazato M, Hammer RE, Saper CB, Yanagisawa M. Narcolepsy in orexin knockout mice: molecular genetics of sleep regulation. *Cell*. 1999 Aug 20; 98(4): 437-51.
- [48] Masamichi Sakagami, Ken-ichiro Tsutsui, Johan Lauwereyns, Masashi Koizumi, Shunsuke Kobayashi and Okihide Hikosaka. A Code for Behavioral Inhibition on the Basis of Color, But Not Motion, in Ventrolateral Prefrontal Cortex of Macaque Monkey. *Journal of Neuroscience* 1 July 2001, 21 (13) 4801-4808;
- [49] Wulff K, Gatti S, Wettstein JG, Foster RG. Sleep and circadian rhythm disruption in psychiatric and neurodegenerative disease. *Nat Rev Neurosci*. 2010 Aug;11(8): 589-99.
- [50] Dement WC, Kleitman N. *J. Exp. Psychol.*, 53, 339 (1957). CAS Article Google Scholar
- [51] Dement WC, Wolpert EA. *J. Exp. Psychol.*, 55, 543 (1958). CAS Article Google Scholar
- [52] Wolpert, E. A., *Arch. Gen. Psychiat.*, 2, 231 (1960).
- [53] Roffwarg, H. P., Dement, W. C., Muzio, J. N., and Fisher, C., *Arch. Gen. Psychiat.*, 7, 235 (1962).
- [54] Oudiette D, Dealberto MJ, Uguccioni G, Golmard JL, Merino-Andreu M, Tafti M, Garma L, Schwartz S, Arnulf I. Dreaming without REM.
- [55] Solms M. Dreaming and REM sleep are controlled by different brain mechanisms. *Behav Brain Sci*. 2000 Dec; 23(6): 843-50.
- [56] Chemelli RM, Willie JT, Sinton CM, Elmquist JK, scammell T, Lee C, Richardson JA, WILLiams SC, Xiong Y et al. Narcolepsy in Orexin knockout mice. *Molecular genetics of sleep regulat Cell* 1999,20:98 [4] : 437-51
- [57] Siclari F, Baird B, Perogamvros L, Bernardi G, LaRocque JJ, Riedner B, Boly M, Postle BR, Tononi G. The neural correlates of dreaming. *Nat Neurosci*. 2017 Jun;20(6):872-878.
- [58] Francesca Siclari, Giulio Bernardi and Giulio Tononi. Dreaming in NREM Sleep: A High-Density EEG Study of Slow Waves and Spindles. *J Neurosci*. 2018 Oct 24; 38(43): 9175–9185.