

# Unveiling sleep mysteries: neurobiology of dreaming

*Revelando mistérios do sono: neurobiologia dos sonhos*

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"Yea, all which it inherit shall dissolve,  
And like this insubstantial pageant faded,  
Leave not a rack behind. We are such stuff  
As dreams are made on, and our little life  
Is rounded with a sleep. Sir, I am vexed.  
Bear with my weakness. My old brain is troubled."

**William Shakespeare's *The Tempest*: act 4 scene 1**

## ABSTRACT

Dreaming is the result of the mental activity of rapid eye movement (REM) sleep stage, and less commonly of non-REM sleep. Dreams offer unique insights into the patients' brains, minds, and emotions. Based on neurophysiological and neuroimaging studies, the biological core of dreaming stands on some brain areas activated or inactivated. Dream abnormalities in neurological disorders include a reduction / cessation of dreaming, an increase in dream frequency, changes in dream contents and accompaniments, and the occurrence of dreamlike experiences (hallucinations) mainly during the wake-sleep/sleep-wake transitions. Dream changes can be associated with several neurological conditions, and the unfolding of biological knowledge about dream experiences can also have significance in clinical practice. Regarding the dream importance in clinical neurological management, the aim of this paper encompasses a summary of sleep stages, dreams neurobiology including brain areas involved in the dreams, memory, and dreams, besides Dreams in the aging people and neurodegenerative disorders.

**Keywords:** dream, REM sleep, narcolepsy, parasomnias, REM sleep behavior disorder, Parkinson's disease, epilepsy, hallucinations

## RESUMO

Sonhar é o resultado da atividade mental do estágio do sono de movimento rápido dos olhos (REM) e, menos comumente, do sono não-REM. Os sonhos oferecem informações únicas sobre o cérebro, a mente e as emoções dos pacientes. Com base em estudos neurofisiológicos e de neuroimagem, o núcleo biológico do sonho está em algumas áreas do cérebro ativadas ou inativadas. As anormalidades do sonho nos distúrbios neurológicos incluem uma redução / cessação do sonho, um aumento na frequência do sonho, alterações nos conteúdos e acompanhamentos do sonho e a ocorrência de experiências semelhantes ao sonho (alucinações), principalmente durante as transições de vigília-sono / sono-vigília. As mudanças do sonho podem estar associadas a várias condições neurológicas, e o desenvolvimento do conhecimento biológico sobre as experiências do sonho também pode ter significado na prática clínica. Com relação à importância do sonho no manejo neurológico clínico, o objetivo deste artigo é resumir os estágios do sono, a neurobiologia dos sonhos, incluindo as áreas do cérebro envolvidas nos sonhos, a memória e os sonhos, além dos sonhos nos idosos e nos distúrbios neurodegenerativos.

**Palavras-chave:** sonho, sono REM, narcolepsia, parasomnias, distúrbio do comportamento do sono REM, doença de Parkinson, epilepsia, alucinações

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## INTRODUCTION

In the process of clearing up the mysteries of sleep, this paper briefly summarizes some issues about the dreams and their brain origins, following the other two articles, about sleep functions and sleep chronotypes.

The conception of dreaming has significantly transformed along to the times, which led to many different theories about its biological and psychological aspects<sup>19</sup>. However, dreams occur at sleep as events internally generated, with reduced control over their content that includes sensory-motor, verbal, cognitive, and emotional experiences with a sense of reality<sup>6,19</sup>.

The dreams are a universal human experience that has fascinated humankind, and they are studied from a neurological, psychiatric, psychological, and philosophical perspective. In particular, lucid dreaming (LD) refers to a state of becoming aware during ongoing sleep dreaming<sup>1, 8, 19</sup>. Indeed, the LD is carried out in a kind of consciousness with features of waking and dreaming states<sup>19</sup>.

Even though the dreams had been addressed from several different perspectives, the one to be here privileged is on neuroscientific studies of the brain-mind system's activities during sleep.

The modern era of dreams research comes during the second half of the 19th century, mainly by Hervey de Saint-Denys. There is also Freud's masterpiece, "The Interpretation of Dreams," that relies exclusively on the manifest psychoanalytic content of the dreams. In 1953, Nathaniel Kleitman and his two students, Eugene Aserinsky and William Dement made a revolutionary discovery about rapid eye movement REM sleep. These REM periods were also found to be related to muscle atonia by Jouvet (1959), thus preventing the dreams from being acted out. Another milestone was made by Hall 1953/1966, who published "The Meaning of Dreams," in which he described and classified the phenomenological characteristics of thousands of dreams. In 1977, Hobson and McCarley presented their work "The brain as a dream state generator..." based on the activation-synthesis model for dream and related physiological characteristics of REM sleep<sup>6</sup>.

A primary drawback to the study of dreams is that an objective evaluation of them is not currently possible, and researchers depend exclusively on the subject's subjective report<sup>19, 21</sup>. There is a gap between the real dream and its description, so the original content of the dream can be distorted due to the interfering waking environment

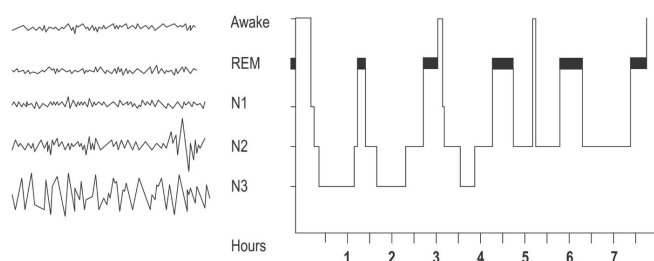
material. Also, there are limitations inherent to verbal reports and moral censorship, as well as, the absence of dreams reports does not necessarily imply their absence since these can be easily and quickly forgotten<sup>19</sup>.

REM and non-REM sleep stages are usually linked to different types of dreams, but a central question of sleep research is where the brain drives dreams' video-auditory experience.

## SLEEP STAGES, DREAMS, AND LUCID DREAMING

The sleep is not homogenous; on the contrary, it is composed of four to six cycles, each one divided into sleep phases, in an eight-hour night sleep of an adult. Indeed, there is a sleep cycling between REM phasic and tonic phases and non-REM sleep 1 to 3, being this rhythm ultradian because it occurs with a frequency of fewer than 24 hours. The polysomnography presents these periods in a diagram called hypnogram (Figure 1). It shows the cycles, each of about 90-minute periods, between deep non-REM sleep and dreaming REM sleep multiple times per evening. Each phase has its own specific EEG patterns and physiological changes. The majority of deep non-REM sleep occurs in the first and second cycles, but as the night develops, the proportion of REM sleep in a cycle increases, and the lighter stage non-REM 2 sleep predominates.

Age has a significant consequence on the total sleep time (TST) and the ratio of non-REM/REM sleep. Besides, neonates have REM sleep of about 50% of TST, and longer sleep time and adults usually sleep 6–8 h per day with 15–20% REM sleep. With increasing age, TST changes little, while sleep is more fragmented with more frequent and more prolonged awakenings, with less REM sleep and more light NREM sleep.



**Figure 1.** A hypnogram of the human sleep macrostructure right, presenting the sleep during eight hours, the cyclic group of sleep stages that comprises N1, N2, N3 – all non-REM rapid eye movement and REM sleep. At the left, the corresponding EEG. Slow-wave sleep N3 prevails in the first half of the night, whereas N2 and REM in the second half of the night. Even though REM sleep usually comes after N2, it is placed higher on the graph since the brain activity is comparable to that of wakefulness.

Dreams can occur during any sleep stage REM and non-REM, albeit less often during non-REM sleep. Especially when a person is awakened from sleep, he/she occasionally recalls dreams and, at times, recalls no experiences. Nevertheless, REM sleep lasts steadily related to higher dream recall than non-REM sleep. Still, differences in study methodology, sleep stage duration, and time of night can impact the content or raise the frequency of dream recall from non-REM sleep. On the whole, the quality of non-REM and REM dream reports differs in steady ways because non-REM dreams are characteristically smaller, more fragmented, and more resembling the process of thought. In comparison, REM dreams are longer, more emotional, and more bizarre<sup>6, 21</sup>. Indeed, dream reports tend to be mainly rich, with complex, emotional, and perceptually vivid experiences after awakenings from REM sleep than from non-REM<sup>6</sup>.

Regarding dreams reports from non-REM sleep waking: stage N1, they are commonplace 80–90% of the time, though they are very short, and usually people report hypnagogic hallucinations; stages N2 and N3 yield reports about some experienced content 50–70% of the time, early in the night, when stage N3, awakenings yield few reports<sup>21</sup>.

Dreaming may be thought-like mentation and intense experiences, the first in non-REM sleep, and the other, typical of REM sleep<sup>6</sup>. Attributes such as length, oddness, and perceptual distinctness increase toward REM sleep. Indeed, dream phenomenology has often been matched with that of psychosis since dreams share significant resemblances with many of the typical features of psychosis and mainly with the positive symptoms of schizophrenia<sup>19</sup>. There are in the dreams and psychosis intrinsic sense perceptions independent of external stimulation, and also, lack of criticism regarding the bizarreness of the experiences<sup>16</sup>. Consequently, both share important neurophysiological and phenomenological features, such as subjective experience.

It is remarkable that human beings typically do not have an awareness when they are dreaming during REM sleep. However, occasionally a notable exception happens, and reflective consciousness can be recovered while dreaming, what is referred to as LD<sup>1</sup>. Regarding its occurrence, LD is not rare, as according Dodet et al.<sup>7</sup>, about 51% of adults in a German representative sample had experienced an LD at least once.

However LD prevalence varies widely from

26-92%, maybe for methodological differences as well socio-demographic and cultural aspects of the studied population<sup>17</sup>.

Besides, LD is more frequent in children than in teenagers and adults<sup>7</sup>. In comparison to non-lucid REM sleep, LD REM sleep is related to local frontal lobe EEG changes in the 40 Hz band, with augmented brain coherence<sup>7</sup>.

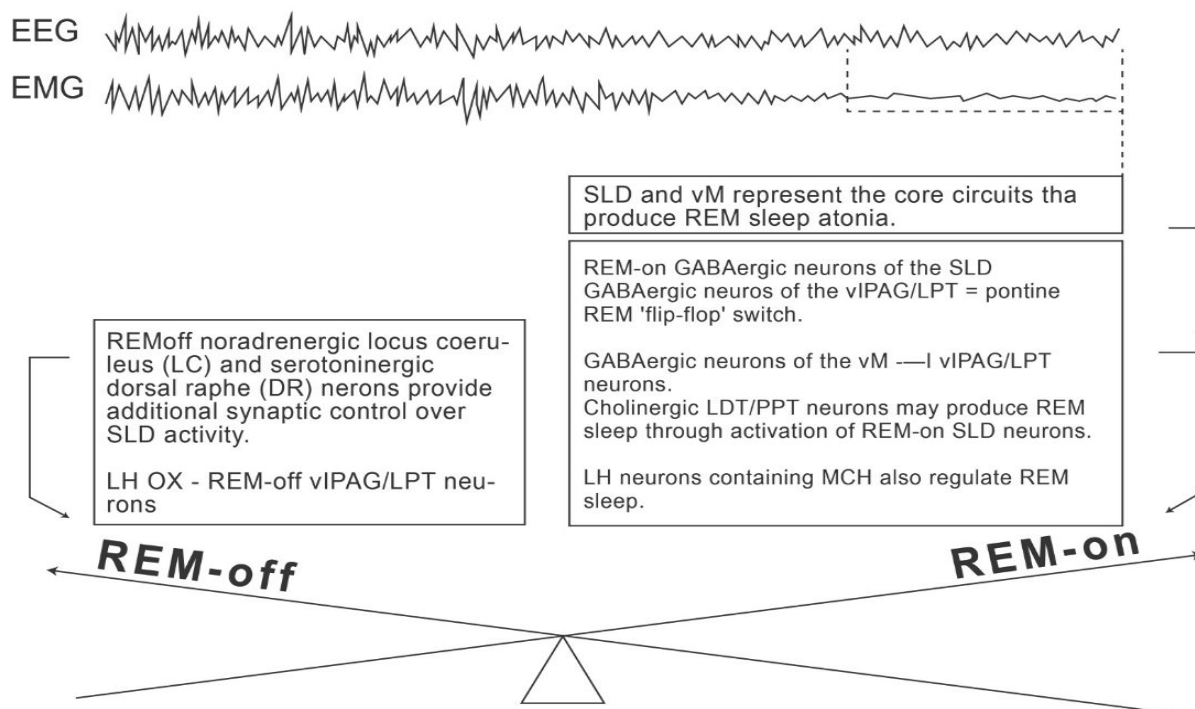
LD is also linked to increased physiological activation, and autonomic nervous system arousal is also found to be elevated during LD REM sleep in comparison to non-LD REM sleep<sup>1</sup>. Besides, LD happens in REM sleep later in the night what suggests that LD is related to augmented cortical activation, and the prefrontal cortex is more active than during regular dreaming<sup>1,16</sup>.

In short, regarding dreaming neurophysiology, the study discoveries suggest that REM sleep might reasonably be considered as a facilitating neurophysiological state for dreaming to occur, even though dreams are not exclusively experienced during this sleep stage<sup>6</sup>. However, REM sleep and dreaming can be detached, because lesions in the forebrain can leave REM sleep intact, whereas dreaming ceases. In contrast, brain stem lesions can stop REM sleep from happening though individuals remain to report dreams after awakening<sup>19</sup>.

The REM sleep is characterized by rapid eye movements, dreaming state in which there is a stimulation of the cortical and hippocampal EEG with a desynchronized electroencephalographic activity where theta activity 4–7 Hz prevails, besides loss of muscle tone that impedes the individual from acting out the action of dreams<sup>14,23</sup>. An insufficiently understood neuronal network is linked with it. However, it is known that there are multiple nuclei and neurotransmission systems that are concerned with sleep muscle paralysis. In wake and REM sleep, the subcortical cholinergic tone is highly active and has a sustained depolarization in cortical neurons and EEG activation<sup>21</sup>.

During sleep, the mammalian brain alternates between two distinct states- REM sleep with a desynchronized EEG and non-REM sleep, characterized by large-amplitude slow-wave activity. For decades, the precise nature of the REM turn-on and off is under investigation. Lu et al.<sup>14</sup> propose that REM organization is based on REM-on/REM-off flip-flop switch reciprocally inhibitory system, GABAergic synaptic projections, between REM-off neurons in the ventrolateral periaqueductal gray and lateral pontine tegmentum - vIPAG/LPT, and REM-on neurons in

the sublateralodorsal nucleus - SLD **Figure 2.**



**Figure 2.** The circuit basis of REM Sleep Flip-Flop Model 23 e Fuller: Abbreviations: sublateralodorsal nucleus SLD, ventral medulla vM, ventrolateral periaqueductal gray and lateral pontine tegmentum vIPAG/LPT, Lateral hypothalamic neurons LH-OX, laterodorsal tegmental and pedunculopontine tegmental LDT/PPT, melanin-concentrating hormone MCH, locus coeruleus LC, dorsal raphe DR neurons.

## BRAIN AREAS INVOLVED IN THE DREAMS

Modern brain imaging techniques have emerged as essential tools to understand better the neural mechanisms of dreaming<sup>6</sup>. Now, it is possible to capture more transient, dynamic changes of brain activity with a high anatomical resolution mainly by functional MRI studies. This can be carried out throughout REM dreams that present the current knowledge of the cerebral correlates of dreaming<sup>6</sup>.

The whole brain is active during dreams, and most dreams occur during REM sleep but also in non-REM sleep. Notably, the limbic system in the mid-brain that includes the amygdala deals with emotions in both waking and dreaming, and it is mostly associated with fear. Regarding the cortex, it is in charge of the content of dreams, but some parts of the frontal lobes are least active. Besides, specific dream characteristics suggest the activation of particular brain regions during sleep<sup>6</sup>.

Siclari et al.<sup>25</sup> studied successive awakenings of subjects recorded during the night with high-density EEG 256 channels. In both non-REM and REM sleep with reports of dream experience, the results highlighted a parieto-occipital 'hot zone' as the neural relate of dreaming. On the dependence of associated reports of experiences or not,

the EEG varies: local decrease in low-frequency EEG activity, in the first, and local increase, in the second. This suggests that it may constitute a significant correlate of conscious experiences in sleep. Indeed, by indicating how dreams burst into similar parts of the brains that involve reality in waking states, Siclari et al.<sup>25</sup> explain dreams as a form of consciousness that occurs during sleep.

The already mentioned study by Siclari et al.<sup>25</sup> identified that the same parts of the brain in charge of certain actions when awake, turn into active when dreams enclosed those specific elements. Besides, the study also revealed that absent or forgotten dream experiences also carry a distinct EEG mark.

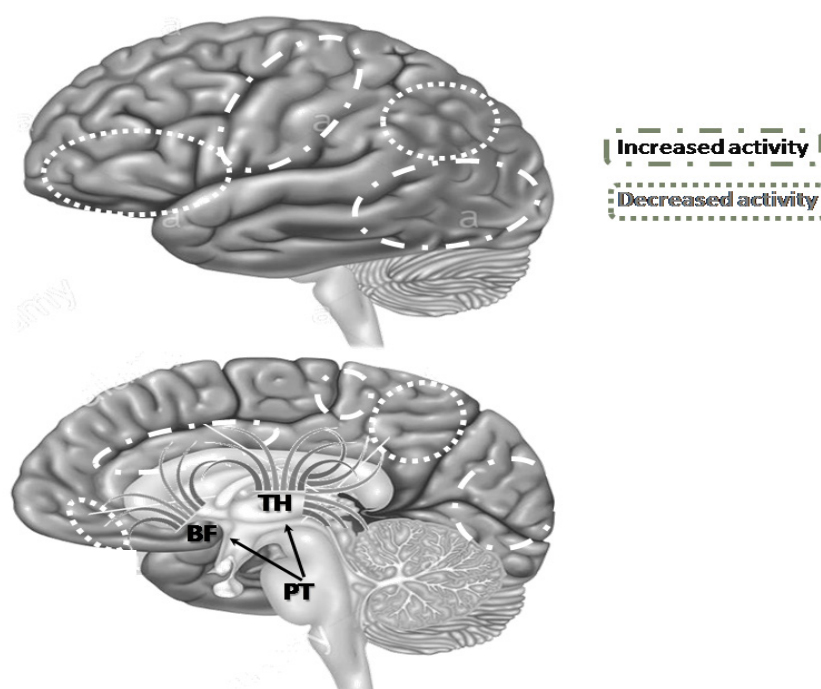
Desseilles et al.<sup>6</sup> reported, based on neuroimaging data, that highly visual content of the dreams are dependable with the widespread activity along occipital-temporal visual regions. Besides, a dream report also contains a significant motor component, which is consistent with activation in motor regions during REM sleep. Several regions are significantly hypoactive during REM sleep when compared to wakefulness, in particular the dorsolateral prefrontal cortex DLPFC, orbitofrontal cortex, posterior cingulate gyrus, precuneus, and the inferior

parietal cortex as remarked by Desseilles et al.<sup>6</sup>. In this way, REM sleep exhibition deep lacking working memory, orientation, and logic with prefrontal and parietal deactivation.

Also, frightening dreams experiences are suggestive of increased amygdala activation during REM sleep. Even though, the neurobiology of LD is still incompletely characterized, because of EEG varied results and because of scant Neuroimaging data, preliminary results suggest that prefrontal and parietal regions are involved in LD<sup>1</sup>. Besides, cortical areas activated during LD show striking overlap with brain regions that are impaired in psychotic

patients, in particular, fronto-parietal regions are involved in both phenomena, according to the study of Dresler et al.<sup>9</sup>.

Consequently, initial evidence proposes that regions of anterior prefrontal, parietal, and temporal cortex are compromised in LD, brain regions involved with metacognitive processes during the waking state<sup>1</sup>. In consequence, LD was linked to a reactivation of areas that are typically deactivated during REM sleep what can elucidate the recovery of reflective cognitive capabilities that are the seal of LD<sup>8</sup>. Besides, these findings may correspond to restored reflective consciousness, as quoted by Dodet et al.<sup>7</sup>.



**Figure 3.** Correspondence between the distribution of activity in REM sleep and typical dream features an adaptation of the Figure by Desseilles et al.<sup>6</sup>. The dreaming brain in REM sleep mainly includes the pontine tegmentum, thalamus, limbic/ paralimbic structures including the amygdala, and temporooccipital areas 2.

Top: Dream report content during REM sleep-related to: 1-activation of highly visual - occipital-temporal visual regions and important motor component - motor regions; 2-deactivation of the frontal lobe and many others, as the inferior parietal cortex. Bottom: Ponto-geniculo-occipital waves (PGO) originating from the pontine tegmentum (PT) mediate some widespread cortical activation via a ventral pathway innervating the basal forebrain (BF) and a dorsal pathway innervating the thalamus (TH). Frightening experiences in dreams are evocative of increased amygdala activation.

## MEMORY AND DREAMS

Although waking experiences are not faithfully replayed in dreams, it is known that events and memories starting on waking period can be merged into dreams, and these integrations can be an exact duplication of what happened in waking life, or, more frequently, they can be partial or indirect<sup>10,3</sup>. Nevertheless, as a whole, the neural mechanisms underlying memory regulation during sleep are not yet fully understood, and it is known that learning experiences influence the content of subsequent sleep mentation such as "dreaming"<sup>12,27</sup>. Besides, post-training

sleep is recognized as beneficial for human memory. This is due throughout the sleep to an iterative "reactivation" of memory networks, synaptic connections, and memory consolidation<sup>27</sup>.

The processing of recent emotional memories, and the number of references to recent waking-life experiences in REM dreams were considered to be positively correlated with frontal theta activity in the most recent 3 min of the REM sleep phase from which the dream was collected. However, this correlation was not detected for older me-

mories<sup>10</sup>.

Eichenlaub et al.<sup>10</sup> remember that the memories establish much of the foundation material for the dreams. Consequently, the authors explored the connection between REM frontal theta and the memory sources of dreaming. Their results suggest that wakefulness-related dream formation content is related to REM theta activity, in concert with theories that dreaming imitates emotional memory processing taking place in REM sleep<sup>10</sup>. Additionally, the emotional amount of recent waking-life experiences incorporated into dreams was higher than the emotional strength of experiences that were not included<sup>10</sup>.

The events and memories from waking life can be incorporated into dreams, and the temporal relationships of them are referred to as the day-residue or immediate incorporation effect<sup>3</sup>. Blagrove et al.<sup>3</sup> study address whether the dream-lag effect occurs only for REM sleep dreams or for both REM and non-REM stage 2 dreams. For this experiment, 20 contributors kept a daily diary for over a week previously sleeping in the sleep laboratory for 2 nights. REM and N2 dreams collected in the laboratory were recorded, and each subject rated the level of correspondence between every dream and diary record. The dream-lag effect was found for REM, but not N2 dreams, this last one being shorter than the REM dream reports. The authors concluded for evidence for a 7-day sleep-dependent non-linear memory consolidation process that is specific to REM sleep, in agreement with the importance of REM sleep to emotional memory consolidation.

In opposition to this idea of memories consolidation in the dreams and REM sleep vital functions of storing memories, there is also the one of actively forgetting memories during dream sleep. To prevent overload, sleep-including REM sleep may actively forget excess information.

Izawa et al.<sup>12</sup> identified neurons in mice that are involved in erasing memories and that hypothalamic MCH neurons actively contribute to it. Besides, activation or inhibition of MCH neurons impaired or improved hippocampus-dependent memory, respectively. The hypothalamus MCH neurons form distinct populations for wake and REM sleep, and the "REM sleep state-dependent inhibition of MCH neurons impaired hippocampus-dependent memory without affecting sleep architecture or quality," as reported by Izawa et al.<sup>12</sup>. The sleep stage when the MCH cells turn on may avoid the content of a dream from being stored in the hippocampus. Consequently, the dream rapi-

dly vanishes. Accordingly, the study results suggest that MCH neurons support the brain actively forget new, perhaps, irrelevant information.

Marzano et al.<sup>15</sup> propose that the fundamental neurophysiological mechanisms for encoding and recall of episodic memories may be similar through diverse states of consciousness. Explicitly, the encoding of dream matters throughout sleep, according to previously mentioned authors, share some electrophysiological aspects with the episodic memories encoding of the awake brain<sup>15</sup>.

## **DREAMS IN THE AGING PEOPLE AND NEUROLOGICAL DISORDERS**

Dream abnormalities in clinical neurology have poorly been studied, but altered dreaming and dreamlike experiences can be of clinical significance because of their prognostic, diagnostic, and therapeutic implications<sup>2</sup>.

The whole literature comes to an understanding that dream recall gradually declines, faster in men than in women, from the beginning of adulthood, besides dream reports become less intense, perceptually and emotionally<sup>11</sup>. These temporal changes may be related to the one in lifestyle and attitude concerning dreams in early adulthood, but mainly by changes in sleep physiology and REM sleep<sup>11</sup>. The most analyzed aspects of dreaming in degenerative cognitive disorders are those of REM sleep behavior disorders, and nightmares induced by cholinesterase inhibitors<sup>11</sup>. Besides, in comparison with healthy aged persons, patients suffering degenerative dementia dream much less, which can be related to the reduction of REM sleep, besides atrophy of brain associative sensory areas<sup>11</sup>.

The dreams changing can be related to their quality and/or quantity or their association. There are those with reduction/cessation of dreaming, an increase in dream frequency, changes in dream contents and accompaniments including REM sleep behavior disorder, and the occurrence of dreamlike experiences hallucinations during wakefulness, and wake-sleep/sleep-wake transitions<sup>2</sup>. The terms Charcot-Wilbrand syndrome and anoneira cessation of dreaming - global anoneira are applied to define the absence of dreaming as a consequence of focal brain damage<sup>2</sup>. In complementation to the dreams disorders classification, disturbed dreaming has been identified as a primary e.g., narcolepsy, nightmares, or secondary symptom in many medical conditions such as stroke or Parkinson's syndrome Figure 4.

The dreams may also occur in patients with sleep

disorders like insomnia, sleep apnea syndrome, narcolepsy. In insomnia, dream recall is heightened, dream reports are more extended, and it may reflect existing stressors. There is an elevated dream-recall frequency in sleep apnea syndrome patients. The nightmares are sleep disorders with dreams embedded in a vivid and disturbing matter that are most prevalent in childhood during REM sleep, of the middle of the night or early morning, but they can occur to adults as well. They usually involve an immediate awakening and good recall of the dream. On the contrary, sleep terror, also common in children, is often very disturbing, but that takes place during non-REM sleep and without good recall of the dream<sup>2</sup>.

The primary source on the neuropsychology of dreaming is a study by Solms (1997) utilizing a Clinico-Anatomical method, as recorded by Nir and Tononi<sup>21</sup>, in their review. Solms examined 361 neurological patients and asked them minutely about their dreaming. Broadly, brain lesion studies indicate that dreaming rests on specific forebrain regions instead of the brainstem REM sleep generator. Global cessation occurs as a result of a lesion in or near the temporo-parieto-occipital junction, more frequently unilaterally than bilaterally, less commonly, follows bilateral lesions of white matter tracts surrounding the frontal horns of the lateral ventricles, the underlying ventromedial prefrontal cortex. Many of these nerve fibers originate or terminate in limbic areas, in line with increased limbic activity in REM sleep, as exposed by functional imaging. Also, more restricted lesions produce the cessation of visual dreaming or the disruption of particular visual dimensions in dreams. Some lesions, especially those in the medial prefrontal cortex, the anterior cingulate cortex, and the basal forebrain, are linked with increased frequency and vividness of dreams and their intrusion into waking life. Though many brain-damaged patients report no changes in dreaming<sup>21</sup>.

Regarding the quality/quantity dream anomalies, they can be classified from one extreme, dream recall ceases entirely or is unusually impoverished in number or content, to other pole. At this side, dreaming is profuse and vivid as can occur with anterior limbic damage and, seldom, as an epileptic phenomenon in temporal lobe seizures epileptic dreams. Besides, dementia and amnesic syndromes can reduce the occurrence and a verbal manifestation of dreams<sup>2</sup>. Besides, intense dreaming may become rigidly repetitive in conditions such as REM sleep behavior disorder (RBD) with or without

parkinsonism, epilepsy, and migraine. Therefore, episodic memories, which are typically absent from dream content, appear more frequently in disturbing dreams<sup>20</sup>. Dreams with amplified vividness, violent/aggressive matters, and increased/uncontrolled motor activity enacted dreams propose the occurrence of an RBD that can occur in the course of neurodegenerative disorders, brainstem lesions, narcolepsy, drug/alcohol abuse and in the so-called parasomnia overlap syndrome<sup>2</sup>. This last one represents the combination of features of arousal disorders with REM sleep behavior disorder<sup>2</sup>.

The sleep-related experiences and hallucinations are non-veridical perceptions that share some brain mechanisms. Still, differences remain as the first are apart from reality, whereas hallucinations are based on veridical perceptions. In consequence, there is insufficient evidence to fully support the notion that the common of hallucinations rest on REM procedures or REM intrusions into waking consciousness<sup>28</sup>.

The unregulated REM sleep system in narcolepsy also manifests itself in more bizarre dreams with more negative tones, with perceptions primarily disconnected from reality, while on the contrary, hallucinations are discrete and overlap with authentic perceptions<sup>28</sup>. Visual hallucinations during wakefulness, at sleep onset and on awakening can happen in healthy subjects along with patients with narcolepsy, migraine, epilepsy, midbrain/thalamic lesions peduncular hallucinosis, lesions causing visual loss Charles Bonnet syndrome, sleep paralysis or Parkinson's syndromes<sup>2</sup>. As Bassetti et al.<sup>2</sup> stated, visual hallucinations are informed by about 25–50% of patients with Parkinson's syndrome and predict a Lewy-body disorder with the participation of the parieto-occipital and limbic cortices<sup>2</sup>. Besides, visual hallucinations are frequent in Alzheimer's disease, about 20% of cases, and dementia with Lewy bodies<sup>2</sup>. Migraine most frequently promotes simple visual hallucinations. Still, complex dreamlike visual hallucinations are less common, and recurring dreams and nightmares have been described as an aura equivalent in patients with migraine<sup>2</sup>. Many other neurological disorders/manifestation presents with disturbed dreams such as Creutzfeldt-Jakob disease, Encephalitis and other CNS infections, Delirium tremens / other withdrawal syndromes, and Guillain-Barré syndrome, e.g.:

Regarding sleep paralysis and LD, both are dissociated experiences related to REM sleep<sup>5</sup>. Coincidentally, some studies worked on LD and narcolepsy, such as those

by Denis and Poerio<sup>5</sup>, Dodet et al.<sup>7</sup>, and Rak et al.<sup>24</sup>. This link is based on LD, or being aware that the individual is dreaming during the dream itself, that is also more common in those with narcolepsy, both linked to REM sleep. Besides, many people with narcolepsy have dreamlike hallucinations, just as they are falling asleep, hypnagogic, or waking up, hypnopompic hallucinations. By definition, hallucinations happen only in the complete waking state. However, there is insufficient evidence to completely support the notion that the majority of them count on REM processes or REM intrusions into waking consciousness<sup>2,28</sup>.

In an online survey with 1928 participants age range: 18-82 years; 53% female by Denis and Poerio<sup>5</sup>, the authors established that dissociative experiences were the only shared positive predictor of both sleep paralysis and LD. However, both experiences showed different associations with other relevant variables of interest, because sleep paralysis was foreseen by sleep quality, anxiety, and life stress.

Another study, this one by Dodet et al.<sup>7</sup>, compared 53 healthy controls to 53 patients with narcolepsy who most often recalled recurring nightmares and dreams. Beside, LD was achieved by 77.4% of narcoleptic patients and 49.1% of controls  $P < 0.05$ . The frequency of cataplexy, hallucinations, sleep paralysis, dyssomnia, HLA positivity, and the severity of sleepiness were similar in narcolepsy with and without LD. The duration of REM sleep was longer, the REM sleep onset latency tended to be shorter, and the percentage of atonia tended to be higher in lucid vs. non-lucid REM sleep; the arousal index and REM density and amplitude were unchanged<sup>7</sup>.

Regarding the assessment of the frequency of recalled dreams, nightmares, and LD in narcolepsy patients paralleled to healthy controls in a study by Rak et al.<sup>24</sup>, narcoleptic patients experienced significantly higher LD compared to controls. Besides, many patients respond positively to the lucidity of dreams in their suffering experienced by nightmares.

RBD is known to herald Parkinson's disease and other synucleinopathic disorders such as dementia with Lewy bodies and multiple system atrophy by up to several years. RBD is characterized by the acting out of dreams that are vivid, intense, and violent what is caused by the absence or reduction of the normal paralysis occurring during REM sleep. Dream-enacting activities were reported differently according to different samples. Based on polysomnographic records, it seems that there is a partial

enactment suggested by elevated levels of muscle tone. Besides, patients do not always recall dream content for specific episodes, maybe because they have reduced dream recall or because some of the dreams lack salience.

Nonetheless, a majority of patients report retrospectively that their dreams are more vivid, violent, action-filled, and nightmarish since the onset of their RBD<sup>20</sup>. Although patients with RBD report more dreams about aggressive interactions, especially as aggressors, than controls, they do not get higher scores on a daytime Aggression Questionnaire. Besides, the themes of the associated dreams are mostly repetitive in their structure and emotional content. The presence of RBD among patients with Parkinson's disease is a risk factor for subsequent hallucinations, and RBD with hallucinations can presage the development of further cognitive impairments. Conventional treatments for Parkinson's disease and other synucleinopathies may be responsible for some changes in a dream, and dosage does not differ between patients who hallucinate and those who do not according to Nielsen<sup>20</sup>.

The Dream Repetition may occur in Epilepsy, and as reported by Nielsen<sup>20</sup>, case studies reveal at least two ways episodic memories for seizure activity may be replicated during dreaming. First, auras, phosphenes, or epileptogenic ictal images may appear in recurrent night dreams. Second, recurrent themes in dreams can arise very close to epileptic seizures.

An exciting aspect is raised by Curot et al.<sup>4</sup> regarding "déjà-rêvé" ("already dreamed"). This is related to the fact that epileptic patients occasionally report experiential phenomena related to a preceding dream they had throughout seizures or electrical brain stimulation (EBS) what would be different from déjà-vu. Indeed for Curot et al.<sup>4</sup>, déjà-rêvé is a generic term for three distinct entities: recollection of a specific dream, reminiscence of a vague dream and of experiences in which the subject feels like they are dreaming. EBS-inducing "episodic-like" and "familiarity-like" déjà-rêvé were frequently placed in the medial temporal lobes, but "Dreamy states" were brought by less specific EBS areas while still linked to the temporal lobes. In this way, the authors reveal that déjà-rêvé is a different entity that is dissimilar from déjà-vu, the historical "dreamy state" definition, and other experiential phenomena. These differences may be relevant for clinical practice, as it points to temporal lobe dysfunction and could be valuable for studying the neural substrates of dreams as emphasized by the authors, Curot et al.<sup>4</sup>.



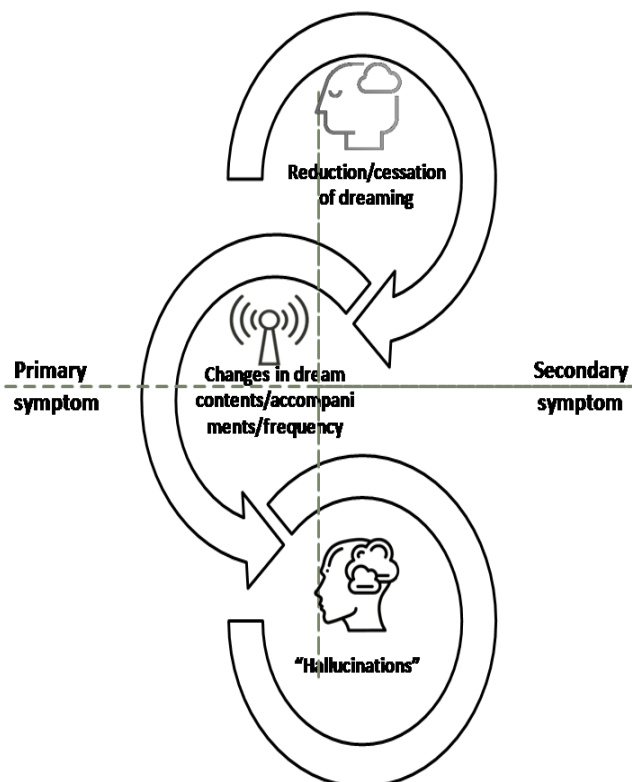


Figure 4. Dream as an expression of clinical neurological significance with intensity/quality and etiology diversity.

## UNFOLDING THE BIOLOGICAL KNOWLEDGE ABOUT THE DREAMS IN NEUROLOGICAL CLINICAL PRACTICE

As disturbed dreaming can be evidence of many medical conditions, its patient's report may be beneficial for a therapeutic approach. In this way, the physician may facilitate the patients to reveal their dream problems regarding frequency and quality. Naturally, the successful treatment also depends upon proper identification of factors responsible for disturbing sleep and dreaming<sup>20</sup>.

Understanding the mechanisms underlying consciousness in the healthy human brain might enable physicians to identify processes that are dysfunctional in many disorders, thereby allowing to develop better treatments. For instance, LD might be of therapeutic value in sleep disorders and for individuals experiencing frequent nightmares, as it will be shown below, and for the treatment of recurrent nightmares in post-traumatic stress disorder<sup>18</sup>.

LaBerge et al.<sup>13</sup> showed that galantamine, with its acetylcholinesterase AChE-inhibiting properties, increases the frequency of LD in a dose-related way. More specifically, the combined method of taking galantamine in the last third of the night with at least 30 minutes of sleep disruption and with a suitably focused mental set is one of the most effective methods for making LD obtainable nowadays, as suggested by LaBerge et al.<sup>13</sup>. Besides,

some evidence suggests that dream lucidity training can be applied in clinical settings as a form of nightmare therapy. Although the mechanism of action of LD is not fully understood, examining the characteristics of patients for whom this type of treatment seems useful may shed light on the nature of LD itself<sup>9</sup>.

Nightmares, hallucinations, and RBD have different prognostic significance, but the distress that they can have for patients and their bed partners must be adequately managed. RBD is also an indication that somebody may be at risk or is vulnerable to neurodegenerative diseases. Therefore it is significant a therapy that can aid patients previously they progress to the neurodegenerative diseases. At the moment, clonazepam suppresses dream-enacting behavior and the disturbing dreams associated with it. Pramipexole and melatonin have partial effects, but melatonin seems to re-establish REM atonia<sup>20</sup>.

Careful drug regimens are of primordial importance as many agents are known or strongly suspected to modify the quality of sleep and dreams. Likewise, stress and anxiety are subject to short-term interventions that can quickly reduce symptoms. Nightmares can occur in patients with psychiatric illnesses, and the assessment of a patient's sleep hygiene can also reveal behaviors that produce fragmentation and sleep deprivation with repercussions on the quality of dreams<sup>20</sup>. Nightmares and night terrors in children usually need education of family members as an essential component of management, besides maintaining a safe environment. Still, pharmacologic intervention is not habitually designated, and behavioral methods for the treatment of recurrent nightmares are effective in older children. Nightmares that occur after a patient's trauma or stress may need psychotherapy and behavioral approaches.

There is a report about the therapeutic approaches of LD training for the treatment of chronic nightmare sufferers<sup>26</sup>. Rak et al.<sup>24</sup> show that many patients with narcolepsy report a positive impact of LD on the distress experienced from nightmares. Therefore, more systematic use of LD has to be well-thought-out as a promising method for treating nightmare symptoms in narcolepsy.

The hypothesis that LD and psychosis insight depends on comparable neural mechanisms needs more evaluation; besides, as awareness of dreaming while it is happening defines LD, it has been proposed to be potentially therapeutic for psychotic patients<sup>9,16</sup>.

Regarding the LD induction devices, it is neces-

sary to prove its effectiveness.

At the same, more scientific studies on other techniques to induce LD are also clearly warranted, as cognitive techniques—such as autosuggestion, reality testing, and alpha feedback, for example; external stimulation—such as light, acoustic, and vibrotactile; and application of donepezil, which is an acetylcholinesterase inhibitor<sup>18</sup>.

In line with this issue, Soffer-Dudek<sup>26</sup> questions the side-effects of LD induction, such as the risk of sleep hygiene and sleep-wake psychological boundaries. This many LD inductions may hypothetically be harmful to mental health because of a possibly sleep disruption quality and reality-fantasy boundaries.

Even though active treatments are accessible for numerous common dream disturbances, the development of new therapies might benefit them, as LD.

## CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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