Università degli Studi di Modena e Reggio Emilia
Facoltà di Medicina e Chirurgia

Corso di Laurea Magistrale in Medicina e Chirurgia
Dipartimento di Scienze Biomediche, Metaboliche e Neuroscienze
Unità Operativa di Neurologia

The language of dreams: a pilot study on dream experience in focal epilepsy

Relatore:

Prof. Stefano Meletti

Correlatrice:

Dott.ssa Alice Ballerini

Tesi di Laurea di:

Amit Oz

Anno Accademico 2024/2025

Index

Abstract

Dreams are a subjective experience generated by our brain during sleep, when we disconnect from the external environment. Although dreams are a universal phenomenon with significant cultural and psychological implications, they remain an enigmatic aspect of our brain function. In recent years, neurological studies have been focused on the relationship between dreams and neurological disorders. However, the connection between dream content and epilepsy, in particular focal epilepsy, remains understudied.

This study aims to investigate the neurological mechanism underlying dream experience in patients with focal epilepsy. We hypothesize that dream experience will be different in patients with focal epilepsy in comparison to a healthy control population, both in oneiric content and in elements of form.

We recruited 19 patients from the Epilepsy Monitoring Unit at Baggiovara Hospital and 15 healthy controls from the IMT School for Advanced Studies in Lucca. Participants were evaluated using cognitive assessment, emotional, and dream-related questionnaires. Only patients underwent a structural MRI.

Analysis revealed significant differences between patients and healthy controls in cognitive assessment, in State-Trait Anxiety Inventory (STAI), Spontaneous Mind Wandering questionnaire (MW-S), and Dream Recall questionnaire (DRQ). Within the patient group, questionnaire scores were correlated with volumes of specific cortico-subcortical regions. STAI and MW-S scores were associated with amygdala volume changes. MW-S scores were also associated with changes in hippocampal volumes. Finally, DRQ seemed more related to different cortical thickness in the medial temporal lobe. This finding suggests a neurological basis for alteration in dream-related experience in individuals with focal epilepsy.

This study shows that patients with focal epilepsy have alterations in cognitive processes and emotional processes that may influence dreaming. Emphasizes that dreams may offer a unique opportunity to evaluate the cognitive alteration in focal epilepsy patients, both as a study tool and as a diagnostic method.

1. Introduction

1.1. Epilepsy

Epilepsy is a chronic neurological disease characterized by recurrent, unprovoked seizures.[1] Although the definition of epilepsy is widely accepted, some aspects are still considered problematic.[2] A seizure is defined by a sudden release of electric energy in the brain.[3] While the disorder is largely described by seizures, it is important to note that experiencing a seizure does not necessarily imply the presence of an epilepsy syndrome.[2] An epilepsy syndrome is a complex diagnosis and can be defined as a combination of features: seizure types, EEG patterns, imaging findings, age of onset, and potential for remission.[4]

The International League Against Epilepsy (ILAE) has recently provided updated criteria for the diagnosis of epilepsy syndrome, based on at least one of these characteristics: (i) at least two unprovoked seizures happening more than 24 hours apart, (ii) one unprovoked seizure with the probability of a second seizure being over 60% over the next 10 years, (iii) confirmed diagnosis of an epilepsy syndrome.[5]

1.1.1. Epidemiology of epilepsy

Epilepsy is considered one of the most common chronic neurological disorders.[6,7] It is estimated that more than 50 million people in the world are diagnosed with epilepsy[1], with approximately 80% of those individuals living in low and middle-income countries (LMICs).[8] Of the total, around 10.5 million are children with active epilepsy, which means that 25% of epilepsy patients are children.[9] In the United States (US), it is estimated that approximately 3 million Americans have active epilepsy, with a lifetime risk of 3%.[10] Other reports estimated that the number of people with epilepsy in the US has increased from 2.3 million to 3 million.[11] In Europe, the prevalence of epilepsy is estimated to be 0.9 million in children and adolescents, 1.9 million among people between 20 and 64 years old, and 0.6 million in the elderly (i.e., over 65 years of age).[12] Epilepsy is frequently linked to various disorders, such as cognitive comorbidities. A verry common association,[13] that can lead to a progressive mental decline, with difficulty in learning, memory, attention, and executing control.[14] Other comorbidities include psychiatric conditions, such as: attention deficit hyperactivity disorder (ADHD), autism, depression, and anxiety. Furthermore, non-neurological or psychiatrically

comorbidities can be associated to epilepsy, including: osteoporosis, sleep disorders, and obesity.[15,16] These comorbidities can have a profound negative impact on social outcome, and quality of life, sometimes more than seizures themselves. Additionally, persistent seizures, in particular in adolescence and young adulthood, are associated with increased mortality, primary due to sudden unexpected death in epilepsy (SUDEP).[17]

1.1.2. Classification of epilepsy

The official classification of epilepsy was first published in 1960, and since then has been revised a few times. The last update of the classification of epilepsy was released in 2025[18], and it contains adjustments based on the clinical application of the 2017 classification[19]. The 2017 commission has created a framework that contains 3 levels: level 1 indicates the main classes, level 2 indicates the seizure type, and level 3 indicates the descriptors. [11]

As presented in **Figure 1**, seizures are first categorized by the onset: focal, generalized, unknown, and unclassified.[19] Focal seizures originate from a specific brain region within one hemisphere.[20,21] The origin can be a localized area or more widely distributed. They can also originate from the subcortical structure. A focal onset seizure can rapidly become bilateral network engagement; in that case, we can refer to the seizure as focal to bilateral tonic-clonic seizure (FBTCS).[20] Generalized seizures are thought to originate from some point within, but rapidly spread in a bilateral way, non-confined to a specific region or one hemisphere.[20] They can include the cortical structure or the subcortical structure, but it is not necessary to include the entire cortex. When there is information available for certain aspects of seizures, but it is insufficient for a clear classification as focal or generalized, it can be referred to as an Unknown onset. In some cases, information regarding seizure onset is lacking; in that case, it can be labeled as Unclassified epilepsy.[20]

The second level describes the seizure type. Patients with focal or unknown seizures can be further classified according to the state of consciousness: it can be labeled as impaired or preserved during the seizure. Consciousness is determined by both awareness and responsiveness,[18] based on information obtained from medical history[22] or through behavioral testing.[23] Rather than asking patients about consciousness, it is preferable to ask specifically about the awareness of the events and the level of responsiveness during the seizure. In the previous version of seizure classification, generalized seizures were categorized into absent

seizures, generalized tonic-clonic seizures, and other generalized seizures.[18] As shown in **Figure 1**[18], tonic-clonic seizures can be positioned in all the main classes: generalized tonic-clonic seizure, FBTCS, and bilateral seizure of unknown origin. In the extended version of the classification, all generalized seizure types are reported, including all types of absent seizures, generalized tonic-clonic seizures, and other generalized seizures. It is recognized that generalized tonic-clonic seizures can be preceded by myoclonic jerks or an absence seizure, in that case it can be referred to as Myoclonic tonic-clonic seizure or Absence-to-tonic-clonic seizure, depending on the form[24].

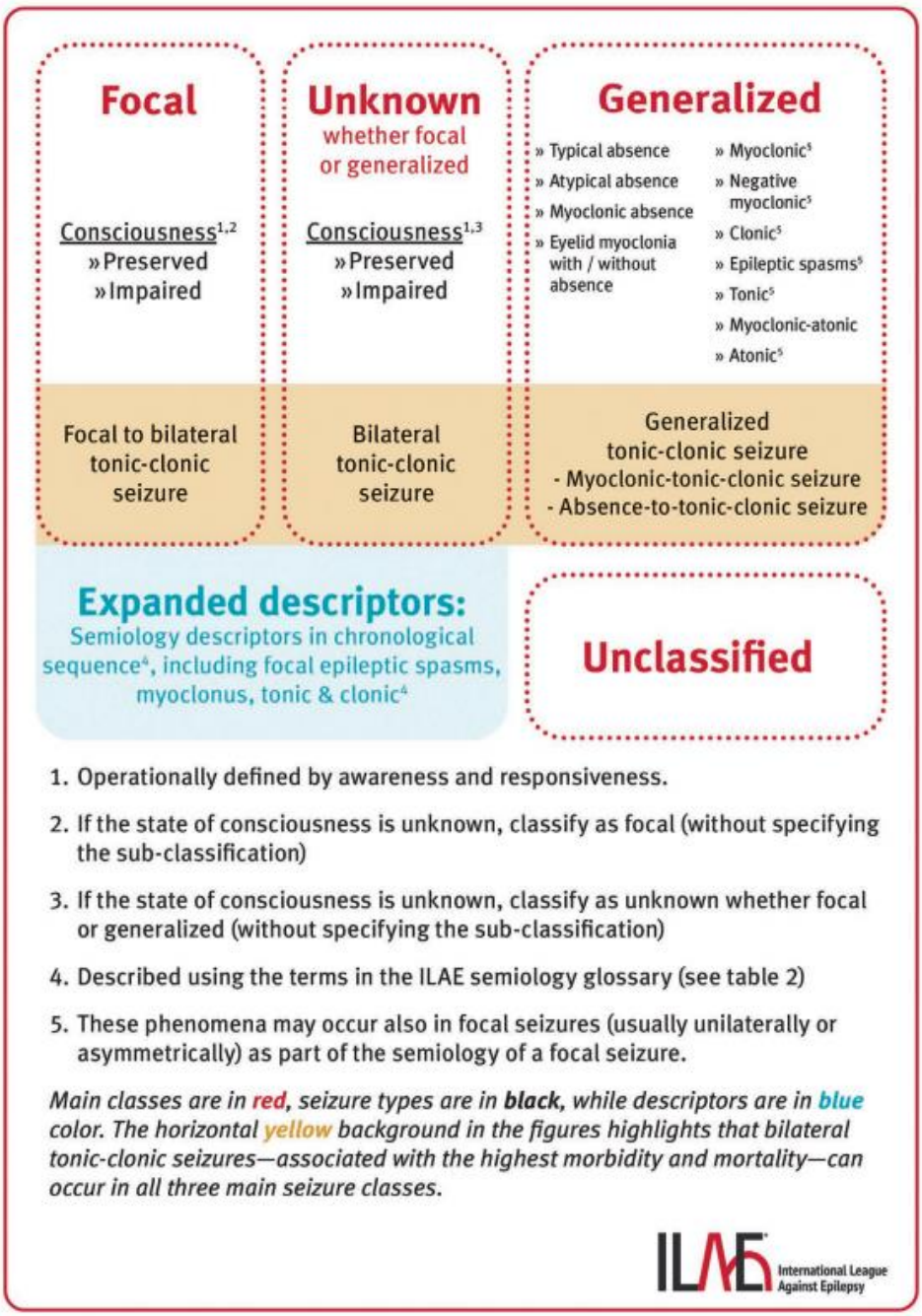

Figure 1: Expanded version of the updated seizure classification (2025)

The third level of the framework is the descriptors. The descriptors contain clinical characteristics of the seizure that are essential for clinical decisions. Seizures are described as having observable manifestations or not. Observable manifestations can include motor, aphasic, autonomic, and other features, and can be easily observed by eyewitnesses.[25] In the extended version of the classification[18], the semiological features are described in chronological order.[26]

1.1.3. Etiology and known causes of epilepsy

As shown in **Figure 2**[27], the 2017 version of the ILAE classification includes etiology along each stage; the consideration of etiology demonstrates the important implication it has on the treatment. Etiology is divided into six groups: structural, genetic, infectious, metabolic, immune, and unknown epilepsy.[27]

When there are visible structural abnormalities at the neuroradiological assessment, the epilepsy could have a structural cause. When the structural abnormalities are combined with electroclinical assessment, it may provide sufficient evidence to conclude that the epilepsy is caused by the structural alteration.[27] The structural lesions may include acquired disorders: stroke, trauma, and infection, or they can be caused by a genetic malformation of cortical development (e.g., focal cortical dysplasia).[28] In some cases, it can be both, for example polymicrogyria may be caused by an inherited genetic mutation, or acquired in an intrauterine cytomegalovirus infection.[29]

In patients with genetic epilepsy, the condition is a direct result of a known or presumed genetic mutation in which seizures are a central feature of the condition. The genetic disorder can be recognized by several sources: first, a family history of an autosomal dominant disorder. For example, in the Benign Familial Neonatal Epilepsy syndrome, most affected families have mutations in potassium channel genes, KCNQ2 or KCNQ3.[30] Secondly, a genetic etiology may be suggested by research in populations with the same syndrome, like Childhood Absence Epilepsy or Juvenile Myoclonic Epilepsy. Furthermore, the same molecular abnormalities can cause varying effects, both severe and mild epilepsy.[27]

The most common etiology on a global scale is infectious etiology. [31] The epilepsy occurs as a result of a known infection, in which seizures are a central feature. This differs from a case of an acute infection, such as meningitis or encephalitis. Common examples can be:

neurocysticercosis, tuberculosis, HIV, cerebral malaria, subacute sclerosing panencephalitis, cerebral toxoplasmosis, and congenital infections such as Zika virus and cytomegalovirus. These infections may have a structural association. [27]

Metabolic etiology means that epilepsy is the result of a known metabolic disorder in which seizures are a primary symptom. The range of metabolic disorders is expanding, and there is a greater understanding of the phenotypic spectrum. These disorders can be referred to as biochemical alterations in the body, such as porphyria, uremia, aminoacidopathies, or pyridoxine-dependent seizures. On many occasions, metabolic disorders can have a genetic mutation, although some may be acquired, like cerebral folate deficiency.

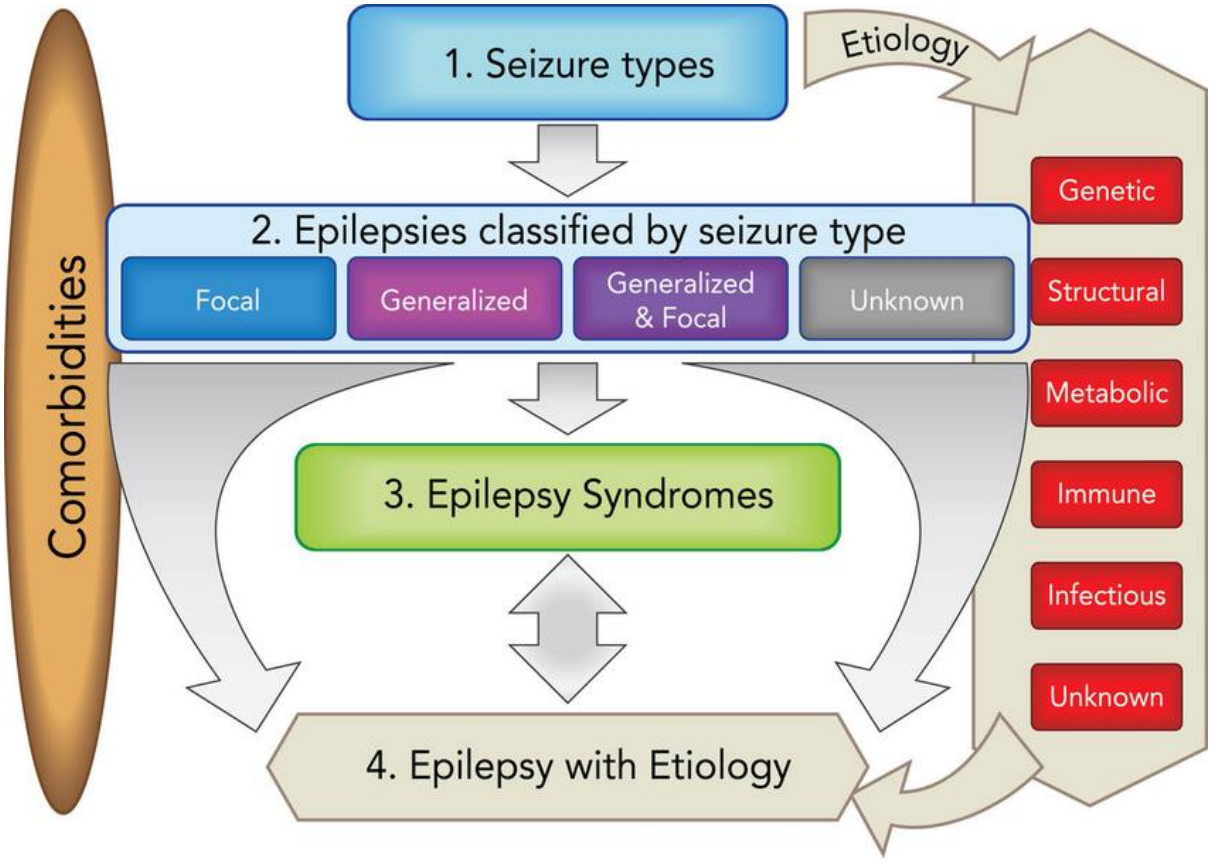

Figure 2: Framework for classification of the epilepsy (2017)

Epilepsy can be the result of an immune disorder. A range of immune disorders have recently been studied and characterized, presenting in both adults and children.[31] In this context, epilepsy is caused by an autoimmune-mediated central nervous system inflammation. Today, the diagnosis of this condition is rapidly increasing, thanks to improved access to antibody testing. For example, anti-NMDA (N-methyl D-aspartate) receptor encephalitis and anti-LGI1 encephalitis.[32]

In some cases, the cause of the epilepsy is unknown, and it is not possible to make a precise diagnosis. The ability to identify the cause varies on the basis of the extent of the evaluation available to the patient, which is influenced by the healthcare setting.[27]

1.1.4. Imaging in epilepsy

Since the electroencephalogram (EEG) offers high temporal resolution of cortical function, it is the central tool in the epilepsy diagnosis process. The EEG is not only used for diagnosing epilepsy, but also to classify focal and generalized seizures. The EEG is a tool used for registration of neural activity inside the human brain.[33] Hans Berger discovered the EEG in the 1920s. Nowadays, advances in computer technologies have led to improvements the EEG acquisition and recording, as well as viewing and analysis.[11] EEG studies are usually performed as routine or prolonged studies (i.e., long-term EEG). Routine EEG is performed for the evaluation of seizures and could include periods of sleep and wakefulness. The total recording period is usually 20-40 minutes, even though longer periods may be necessary for the assessment of interictal epileptiform discharges. Interictal EEG findings in patients with epilepsy can be either normal or abnormal. Abnormal manifestations can include non-epileptic abnormalities, such as slowing, and interictal epileptiform discharges (IEDs).[34] Although IEDs are fundamental for the evaluation of the patient, ictal EEG recordings are the most important part for accuracy in localizing the epileptogenic zone (EZ), as well as for presurgical evaluation. Localizing a seizure onset can be challenging, contributing factors include: a large size of the EZ, rapid ictal discharge progression, or the presence of attenuation in focal onset seizure. In localized seizures, the presence of beta frequency discharge can be present. In generalized onset seizure, the onset includes all EEG derivations simultaneously, although the amplitude of the discharge may be maximal in certain regions. Common generalized ictal patterns are characterized by 3 Hz spike-and-wave, slow spike-and-wave, or atypical spike-and-wave, paroxysmal fast activity, generalized repetitive sharp waves, generalized rhythmic slow waves, and electrodecrement. Often, the seizure involves progression from one pattern to another. Although conventional EEG analysis is adequate to classify the type of epilepsy, it cannot be used to identify the EZ with precision. For this limitation, EEG source imaging (ESI) techniques have been developed. ESI can directly estimate the cerebral generators of surface-recorded electrical fields, allowing a more precise determination of the underlying sources.[35]

Neuroimaging is often needed to determine the etiology and prognosis of epilepsy patients. It plays a key role in identifying the type of epilepsy, and in guiding the selection of appropriate pharmacological therapy. Neuroimaging is also crucial for detecting potentially epileptogenic lesions that may require surgery.[11] The main neuroimaging tools are: computerized tomography and magnetic resonance imaging.

Computerized tomography (CT) has lower sensitivity and specificity compared to magnetic resonance imaging (MRI). It can be used for critical patients, because it takes less time and costs less than an MRI. CT can detect intracranial hemorrhage, but it can miss the presence of small amounts of blood or early non-hemorrhagic infarct.[36] Calcified epileptogenic lesions, cysts and ventricular deformities can be detected by CT. However, CT has limited sensitivity in detecting neuronal migration disorders, hippocampal sclerosis, small tumors, and vascular malformations. Additionally, CT often fails to recognize other brain abnormalities, such as white matter alterations.

MRI is the most sensitive and specific structural neuroimaging test in epilepsy patients with focal epilepsy. MRI is used to select favorable candidates for epilepsy resection surgery, to plan the extent of intracranial monitoring, and to guide subsequent surgical excision or minimally invasive therapies. In patients with structural lesions, approximately 70% achieve post-surgical seizure freedom. However, for MRI-negative patients, post-surgical freedom drops to 46%. The rate of seizure freedom is similar in both adults and children, as well as in temporal and extratemporal epilepsy.[37] The introduction of high-field magnet at 3T, combined with the use of multiple phased arrays instead of conventional quadrature coils, has led to faster image acquisition, enhanced signal-to-noise ratio, and improved image contrast.[38]

Structural MRI is specifically useful in the management of focal patients. Among focal epilepsies, temporal lobe epilepsy (TLE) is particularly significant for its high prevalence and characteristic findings in MRI. In TLE, the most frequent finding is mesial temporal sclerosis (MTS), which is characterized by cell loss and astrocytic gliosis in the medial temporal structures, especially in the hippocampus.[39] However, cell loss and gliosis have also been found in the amygdala, entorhinal cortex, temporopolar cortex, and the temporal pole.[40] At the same time, focal cortical dysplasia (FCD) is a brain malformation that can cause many focal syndromes (e.g., usually temporal or frontal lobe epilepsies). FCD is commonly associated with epilepsy in children, accounting for approximately 26% of intractable epilepsy in children.[41] FCD represents unique challenges in detecting and managing, since it commonly causes drug-

resistant epilepsy and is a frequent histological finding in patients undergoing epilepsy surgery.[42] FCD can be subtle and challenging to detect with standard MRI. The MRI features of FCD typically include: abnormal cortical thickness, abnormal sulcal pattern, blurring of the gray-white matter junction, and abnormal signal in the white and/or gray matter.[41]

1.1.5 Therapy

In 70% of patients with epilepsy, anti-seizure medications (ASMs) may provide good seizure control. An accurate diagnosis of the type of epilepsy, rather than the seizure type, is crucial for selecting the best treatment. However, there are factors that need to be considered for choosing medication: which side effects can be tolerated, other illnesses they may have and which delivery method is acceptable, concurrent medical therapies, drug–drug interaction potential, gender, age, ease of use, clinical urgency, and cost.[43] Over the last 30 years, there has been an increase in the number of ASMs available. Nowadays, there are more than 25 ASMs in the market.[44] In 2015, the American Academy of Neurology (AAN) and American Epilepsy Society (AES) released an evidence-based guideline for managing patients after first unprovoked seizure. One of the conclusions made in this study regards the risk of seizure recurrence, which is greater in the first 2 years, while immediate ASM therapy is likely to reduce recurrence in the first 2 years.[45] The majority of adult patients with newly diagnosed focal epilepsy are initially prescribed monotherapy with levetiracetam (LEV) or lamotrigine (LTG). The majority of them remained on the first ASM throughout the follow-up period.[46] If LEV or LTG were not available, then carbamazepine should be used as an alternative first-line treatment. If the first monotherapy is not successful, a second-line therapy must be accessed; drugs like Lacosamide can be offered as second-line monotherapy. If ASM is unsuccessful, in patients with focal onset seizures, an alternative treatment should be considered.[47] First-line therapy for generalized onset should include LEV or LTG, or valproic acid (sodium valproate). Moreover, LEV and LTG should be offered in first-line therapy in women and girls of childbearing potential. Valproic acid is not recommended in women and girls with the potential of pregnancy, due to its high risk of causing birth defects and neurodevelopmental disorders. If the 3 common use drugs (i.e., LEV, LTG, and valproic acid) are not available for generalized onset seizure, monotherapy with either phenytoin or phenobarbital can be considered.[47]

Studies estimate that between 20% and 70% of individuals with focal epilepsy do not become seizure-free, despite optimal drug therapy. In these cases, if the epileptogenic zone can be

located, surgical resection offers the main potential therapy and a significant improvement in quality of life.[48] The intervention involves localizing the EZ and then removing it surgically, only if the potential benefit outweighs the risk. To localize the EZ, the main investigation tool is MRI, coupled with the use of EEG findings and seizure semiology. The key is to accurately localize the EZ to an area that can be safely removed without causing neurological or cognitive damage. When the lesion is not well defined, further imaging is required, such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT). Good outcome of the surgery appeared to be associated with various factors, such as: preoperative identification of hippocampal sclerosis, an anterior temporal localization of interictal epileptiform activity, the absence of pre-operative generalized seizures, and the absence of seizures in the first postoperative week.[49]

Drug resistance is an important part of determining whether a patient is suitable for presurgical evaluation. Drug-resistant epilepsy is defined as the persistence of unprovoked seizures despite appropriate trials of at least two ASMs, used alone or in combination.[50] This definition is supported by well-established data that demonstrate that a patient with epilepsy is unlikely to achieve seizure freedom using medication alone after failing the two medication trials. Therefore, patients who are proven to be drug-resistant should be considered for epilepsy surgery. Another problem to consider is tolerability, which is a common issue with ASM, with approximately one-third of patients with epilepsy reporting a significant impact on their quality of life.[51] Understandably, intolerable side effects can result in changing medications in an attempt to find more tolerable treatments. While such an event is common, it should be kept in mind that medication failure is defined by the lack of seizure control, and not by intolerance. In rare situations, even patients who correctly respond to the ASM can be considered for epilepsy surgery. For example, if they are at risk of SUDEP, or if the EZ is consistent with a high likelihood of seizure freedom following surgery.[11]

1.2. Dreams

1.2.1. Definitions and theories of dreams

There are a lot of ways to define dreams, the most common definition of dreams is sleep-dependent cognitions. They are thoughts and mental images that occur during sleep. By this definition, for dreams to occur they require sleep. Indeed, rapid eye-movement (REM) sleep

can emerge into daytime consciousness, we may experience dreams or dreamy thoughts and images while awake, commonly referred to as daydreaming. Even if we cannot strictly define dreams as a sleep-dependent condition, we can claim that dreams are highly associated with REM state, which is normally activated during sleep. Dreams occur typically during sleep, and we can define sleep as a restorative process that is brain state-regulated, characterized by reversibility, homeostasis, integration within circadian and social physiology, involving a species-specific quiescent posture and some amount of perceptual disengagement and elevated arousal thresholds. Dreaming refers to a condition that occurs within this biological framework, which is characterized by all the elements mentioned above.[52]

When defining dreams as sleep-related cognitions, it is helpful to clarify the term "cognition". Cognition includes everything that is part of mental life: thoughts, mentions, affects, images, emotions, visual simulations, memories, etc. Although not all forms of mental activities occur in dreams, studies have shown that reading, writing, arithmetic, and reflective thought rarely occur in dreams as compared to their frequency in waking life. On the other hand, certain mental experiences are more common in dreams than in waking consciousness. Additionally, dreams facilitate connections between unrelated concepts; this ability to make connections where the "waking mind" sees no connection, underpins the role of dreams in promoting creativity.

In psychoanalysis fields, there are a variety of theories about dreams. In 1900, Freud considered dreams as a form of "wish fulfillment", as they represent the unconscious desires, thoughts, and motivations that our conscious mind represses.[53] According to Freud, during dreams, subjects could act out desires that they cannot fulfill in waking life. However, certain types of dreams (e.g., dreams that involve punishment or traumatic events) challenge this model. These exceptions led Freud to theories that dreams could also serve as a mechanism for expressing guilt or processing trauma. Ultimately, these insights shaped Freud's revolutionary theory of dreams, suggesting that they are the manifestation of the unconscious processing of the brain.[54] Jouvet hypothesized from a psychological individualization, suggesting that dreams allow genes to express during the night, when there are fewer cultural pressures. [55]

From a neurophysiological point-of-view, J. Allan Hobson and Robert W. McCarley after the discovery of REM sleep in the 1970s, studied animal models. they discover that during sleep there is a network activation that integrates sensory data generated by the reticular, vestibular, and oculomotor neurons in the brainstem. The author theorized that the brain naturally reacts

by attempting to make sense of random stimuli. Thus, dreams have no intrinsic meaning, they serve merely as a side effect of the brain's normal activity. [56]

Other studies suggest that dreams are a cognitive function.[57] Some authors define dreams as "repair mode", as means of solving daily difficulties.[58] Other, as a process in which unnecessary connections in the brain are broken, such as hippocampal consolidation process.[57] Recent studies suggest that dreaming could be a reflection of the consolidation of memory during sleep.[59] Early studies have made a correlation between waking experience and dream content.[60] Moreover, psychology and neuroscience suggested that reactivation of memory during sleep helps the consolidation process, in both animal and human studies. [59]

Despite the numerous theories, no consensus has been reached because testing the impact of dreams on the waking mind and behavior remains a significant challenge.[61]

1.2.2. Neural basis of dreams

Modern studies have shed light on the neuronal basis of dreaming. Traditionally, dreaming has been associated with REM, characterized by “wake-like” activation, with high-frequency electroencephalography activity. However, recent findings indicate that dreaming can occur even in non-REM (NREM) sleep, with a low-frequency activity.[62] This new knowledge has changed the previous concept of neuronal activities during dreams. Indeed, dreams were associated with an activated EEG state (typical REM state), and the absence of dream experience with low-frequency activity (typical in NREM state). Siclari et al. (2017),[63] evaluated participants by EEG in both NREM and REM sleep. Key findings from this study include the identification of a posterior cortical “hot zone”, where a local decrease in low frequency during NREM and REM sleep is associated with reports of dreaming, whereas a local increase in low frequency activity is linked to the absence of dream experience. In addition, results have shown that the location of high-frequency EEG activity is correlated with particular dream contents, such as thoughts, perceptions, and faces.[63] REM sleep is associated with dream reports that are more reliably elicited. While reports after awakenings from NREM stages tend to be shorter, less emotional, and less visually vivid, in comparison with REM sleep reports.[52]

Observation of the anatomical correlation of dreams is primarily made by studies that address the consequences of brainstem lesions and focal cortical damage on perceptual, emotional, and

structural aspects of dream content.[64,65] The general hypothesis is that lesions to pontine brainstem areas reduce or suppress both REM sleep and dreaming.[66] Solms and colleagues critically examined patients with brainstem lesions and the presence of REM sleep. Their review showed a drastic reduction of REM sleep and a complete dream loss in only 1 out of 26 subjects[67]. The authors referred to this case as Charcot-Wilbrand syndrome, which indicate the loss of dreaming after brain damage[68]. Other studies have examined how subcortical and cortical lesions affect dreaming, revealing insights into the neuronal substrates of dreaming. For instance, patients with bilateral basal ganglia damage reported very simple dreams after REM sleep.[69] This suggests that the basic dream imagery is generated by brainstem stimulation and sent to the sensory cortex, while "full dreams" rely on cortical areas for interpretation and integration, subserving higher-order cognitive processes. Other examples can be made with cortical lesions; several reviews on the outcome of acute cortical lesions have shown that unilateral or bilateral injuries are often linked to a complete dream loss.[67,70,71]

Clinical studies highlighted two major brain systems responsible for dream generation. Primarily, the posterior system lesions – especially in the right hemisphere – often effect dreaming and waking visual imagery.[72] Damage to specific regions, such as V4 or V5, affects the representation of colors in dreams or movement.[73] This finding suggests that dream experience shares neuronal mechanisms with visual imagery and visual perception in its late stage of elaboration. The other system involved is the bilateral anterior system, which includes the ventromedial prefrontal cortex (vmPFC) and the white matter surrounding the anterior horns of the lateral ventricles. Lesions to this white matter area, in particular the tracts surrounding the anterior horns of the lateral ventricles and underlying the vmPFC, are less frequently associated with dream cessation. Many of the fibers from these areas originated or terminated in the limbic system.[67,74] Moreover, the ventromedial white matter contains dopaminergic projections, and damage to this area, such as in the case of prefrontal lobotomy, often results in the cessation of dreaming. [67] In addition, damage to the secondary visual areas of the medial occipital lobe/lingual gyrus usually leaves dreams intact, but results in cessation of visual dream imagery. On the other hand, lesions to medial prefrontal cortex (mPFC), anterior cingulate cortex (ACC) and basal forebrain often increase the frequency and vividness of dreams and may cause intrusion into waking life. [75]

Prospective studies on brain-damaged patients are valuable for further understanding the neuronal basis of dreaming, as about 50% of the patients recover the ability to recall dreams at 2-4 years of follow-up.[76] Nevertheless, the relationships between sleep normalization, neuronal

reorganization, and changes in dream recall and/or perceptual properties of dream remain mainly unexplored.

1.2.3. Dreams in neuroimaging

Technological advances have deeper our knowledge of dreams, brain imaging such as PET SPEC, structural, and functional MRI (fMRI), have been used to study the relationship between specific dream features and brain activity during sleep.[77]

The first study that used PET and EEG for evaluating the presence or absence of dream recall showed an activation during REM sleep in the pontine tegmentum, left thalamus, both amygdaloid complexes, ACC, and right parietal operculum. Simultaneously, the study showed a deactivation in extensive regions of the dorsolateral prefrontal cortex (dlPFC), parietal cortex (supramarginal gyrus), posterior cingulate cortex, and precuneus.[78,79] These results align with clinical observation, which indicates that lesions in these areas do not affect dreaming.

Two recent studies, which don't involve dream reports, revealed pronounced activation of the high-order occipitotemporal visual cortex, aligning with the vividness of many dreams, alongside reduced activation in the primary visual cortex during REM sleep. This finding suggests that a high-order visual processing occurs during sleep, without external visual input and a decreased activity of the primary visual cortex (V1).[80,81]

Most subsequent neuroimaging studies have shown a significant difference in brain activity between REM and NREM sleep. REM sleep is characterized by increased activation in regions such as the pons and midbrain, thalamus, basal ganglia, hypothalamus, ventral striatum, visual association cortices, midline limbic and paralimbic areas, as well as in orbitofrontal and paracingulate cortices and part of the mPFC.[79,81] Whereas the dlPFC remains deactivated during the transition from NREM to REM sleep.[79,80,82] These findings encourage a reevaluation of the relationship between brain activity changes and dreaming. Other approaches to evaluating the neural correlation of dreaming are comparing neuroimaging data of brain activity during sleep and resting wakefulness. Dream-like features such as visual imagery and bizarreness have long been noted not only during stage 2 NREM at sleep onset [83], late in night [84], and early in the morning [85], but also during states of relaxed wakefulness. [86] Regarding the default mode network (DMN), studies have shown that both increased [87] and decreased [88] connectivity between its nodes during sleep, suggesting that it has a distinct role in dream

generation.[89] The hippocampal formation, which is more active in REM than NREM sleep, may support the generation of dreams.[90] Meanwhile, the dmPFC, which showed incomplete connectivity during REM sleep[91], might contribute to the lack of insight into the current mental state, leading to the delusional acceptance of dreams as reality compared to waking cognition.[92] Lesion and neuroimaging studies have contributed to the creation of models of the neurobiological bases of dreaming [93,94]. These models converge on identifying brain networks that modulate distinctive characteristics of dreams and dreamlike mental activity [92,95]. Emotional features can be associated with the activation of the amygdala complex, anterior cingulate cortex, and orbitofrontal cortex. Visual imagery can be associated with increased activity occipitotemporal visual cortex. Cognitive alterations can be associated with relative hypoactivation of the dlPFC, and are characterized by alteration of logical reasoning, working memory, episodic memory, and executive functions commonly observed in REM sleep dreams. Memory integration can be associated with activation of mesial temporal areas, specifically the hippocampus. This connection is thought to underlie the incorporation of episodic memories into dream content. Notably, the involvement of the emotional (amygdala, anterior cingulate, orbitofrontal) and visual (occipitotemporal) networks is consistent with the result of brain lesion studies. Additionally, the role of mesial temporal regions is supported by recent electrophysiological[96], neuroimaging [97] , and morpho-anatomical research.[98,99]

1.2.4. Dreams in neurological disorders

Advances in neuroimaging and diagnostic technologies have enabled researchers to link dream characteristics to specific brain activities. [61] The study of various neurological disorders can contribute to our understanding of the underlying mechanisms of dreaming. Another crucial element to evaluate is the diagnostic significance of dreams in relation to sleep and neurological disorders.

In REM sleep disorders, normal REM sleep is associated with the loss of muscle tone (i.e., atonia), regulated with an active inhibitory mechanism in the pons and medulla. When this mechanism is compromised, patients may exhibit dream enactment and nightmares, characterized by movement, facial expressions, vocalizations, and behaviors during REM sleep.[100] Patients awakened immediately after such episodes often describe dreams aligned with their behaviors before awakening.[101] These patients can be injured by the behavior that is activated during sleep, as violent movements, such as kicking, boxing, and jumping, can take

place.[100] It is important to mention that many patients with REM disorders eventually develop Parkinsonism or Dementia, almost always associated with synucleinopathy (i.e., Parkinson's Disease, Dementia with Lewy Bodies, and multiple systemic atrophy). Approximately half of these patients progress to such a condition within 8 years.[102] They often exhibit numerous mild non-motor symptoms, such as hyposmia and constipation, and mildly abnormal test results. These features place them on the spectrum between healthy individuals and patients with Parkinson's disease. The condition is associated with neural loss in the subcoeruleus nucleus in the pons.[103] This knowledge can be used for diagnosis. A screening question, such as *"Have you ever been told, or suspected yourself, that you 'act out your dreams' while asleep?"*[104] is both sensitive and specific for distinguishing REM sleep behavior disorders (RBD) from non-RBD individuals, and patients with sleep apnea.[104] Approximately 93% of patients with RBD report experiencing enacted dreams.[105] Common dream scenarios include being attacked or chased by a person or animal, arguing or falling off a cliff, or defending themselves or loved ones.[106,107]

Patients with Parkinson's disease and Dementia with Lewy Bodies often experience various sleep disturbances, including insomnia, excessive daytime sleepiness, and nightmares. Approximately, one-third of patients report vivid dreams and frequent nightmares, in particular after starting dopaminergic therapy.[108] Their dreams tend to exhibit lower emotional intensity and bizarre contents, which correlated with amygdala volumes and mesial prefrontal cortex thickness. [109] While the correlation with the amygdala involves both hemispheres, only the left mPFC shows an important association with features of dreams[98]. The most notable sleep-related issue in these diseases is the prevalence of RBD which can affect up to 60% of patients[110], and is a strong predictor of future hallucination, psychosis, and dementia.[111,112]

Researchers initially assumed that NREM parasomnias are not associated with dreaming. Recent studies show that 71-77% with NREM parasomnia experience at least one dreamlike mentation associated with a parasomnia episode in their lifetime.[113,114] This experience is different from RBD, and can help to distinguish between these two conditions in the diagnostic process. In NREM parasomnia, dreamlike experiences are typically short, featuring a single visual scene with negative emotions, such as fear and terror. Common themes involve escaping danger or a closed location, imminent death, misfortunes, and disasters.[106,113,114]

Narcolepsy is caused by a deficit in hypocretin, which disrupts the sleep-wake cycle, leading to excessive daytime sleepiness, cataplexy, and sleep onset REM periods.[115] Patient with

narcolepsy report higher dream recall, compared to controls.[116,117] Although, in other awaking conditions, such as sleep laboratory, they show similar frequency of dream recall to those of the control group[118]. The content of the dreams is reported as more vivid, clear, and bright, with more emotions involved, often containing more negative emotions[119]. Nightmares and recurrent dreams are also more common, with 33-70% of patients reporting frequent nightmares.[116,117] Sleep paralysis is significantly common in these patients, occurring in 59% of narcolepsy patients, higher than the healthy controls (15%). Hypnagogic and hypnopompic hallucinations, often related to sleep paralysis, are also frequent. [116] These phenomena can sometimes cause dream reality confusion, where patients may act on hallucinations.[120] Around 77-78% of narcolepsy patients report having lucid dreams (i.e., dreams in which the dreamer is aware of the fact that he is dreaming, and often can influence the dream content[121]), with an average of 7 lucid dreams per month.[116,117] This ability may be linked to frequent transition into REM sleep directly from wakefulness; this kind of transition can allow a higher level of consciousness to be maintained. Patients can often use this ability to take control over dream scenarios in nightmares. Lucid dreaming is associated with creativity, and indeed, narcolepsy patients are often more creative than controls[122], potentially using dreams to incubate original ideas.

This new information, regarding the correlation between neurological disorders and dreams, can be used in the future to improve the diagnostic process. For example, RBD is now recognized as an early indicator for neurodegenerative conditions, such as Parkinson's Disease or dementia with Lewy bodies. Patients with dream enactment need to be further studied and evaluated. Future research should focus on refining these diagnostic tools and exploring the therapeutic possibilities of dream-related conditions in neurological disorders.

1.3. Epilepsy and dream experience

The correlation between epilepsy and sleep alteration is widely reported in the literature. Some types of epilepsy tend to disrupt the micro- and macro-structure of sleep[123]. Tian et al. (2021) found that patients with partial epilepsy are twice as likely to report sleep disturbance in a period of 6 months, compared to a control group.[124] Nocturnal seizures disrupt sleep structure and cause a brief awakening, these brief disruptions can interrupt the sleep structure.[125] Another key component in sleep disruptions in epilepsy patients are the ASMs. For example, first-

generation ASM (e.g., barbiturates, benzodiazepines, phenytoin, and phenobarbital) tend to reduce the time of REM sleep and slow wave sleep.[126] The loss of REM sleep, which can be considered an essential sleep stage, is increasingly recognized as crucial for the consolidation of memory, which impacts daily functioning.[125] The newer generation of ASMs tend to cause less alteration of sleep cycle and architecture. Additionally, there is more evidence of comorbidity between epilepsy and sleep disorders; an example of such patterns has been found between nocturnal frontal lobe epilepsy (NFLE) and NREM arousal parasomnias.[127]

It is logical to assume that epilepsy can have an impact on sleep-related cognitive activity, such as memory consolidation, stimulus integration or perception, and dreaming.[128] The cognitive process is not yet fully understood; nevertheless, by analyzing dream reports, this process has been seen to include sensory and associative functions, short- and long-term memory, executive and emotional processes, mind-reading, and consciousness. Nearly all the cognitive functions used during wakefulness.[129]

Epilepsy can interfere with this process in many ways. It can change the ability to remember dreams, potentially due to dysfunction in brain regions essential for the formation and/or recall of dream memories, involving the medial prefrontal cortex and temporal-parieto-occipital junction.[74,130] In one study by Bentes et al. (2011), epilepsy patients has been proven to have di ability to recall their dreams, but the rate of dream recall is lower than the one in the control group.[131] In patients with focal impaired awareness seizures, dream recall frequency (DRF) was found to be higher for REM compared with NREM awakening, with proportions that are typically seen in healthy individuals. This suggests a specific impairment of NREM sleep dream recall in patients. However, the length and structural organization of dreams did not differ.[132]

Seizures can impact the content of dreams, incorporating elements of seizures into dream content, which happens especially when seizures occur during the night.[128] This is supported by clinical observation, as patients with nocturnal temporal seizures often report having a seizure within their dream, or report a subjective feeling associated with seizures.[133,134]

Solms suggests that focal epilepsy activity could also be a key component in the activation of the mPFC, leading to increased mesocortical dopaminergic activity, which is thought to be involved in the activation of limbic structures during dreaming.[74] This mechanism can link the occurrence of nightmares in patients with nocturnal ictal activity. [135]

Interestingly, previously experienced dreams can be a component of the subject's cognition during diurnal seizure, particularly during temporal lobe seizure, and it is referred to as *"déjà-rêvé"*[136]. The author describes three distinct types of experiences: (1) the recall of a specific and detailed dream with a precise date, resembling episodic memory; (2) the remembrance of a vague dream or element of a dream; and (3) a resembling feeling of a dream.

The first two phenomena are primarily triggered by activation of the medial temporal lobe, while the last one lacks specific anatomical triggers.[136] The clear identification of dream-related memories raises questions about the neuronal system involved in both dream and waking memory. Normally, dream memories are not confused with memories of waking life. This suggests that during elaboration of dream memory, a "dream tag" might be added to the memory, or that the dream-memory system is distinct from the waking-memory system.[128]

A study by Paiva et al. (2011)[137] found that dream reports in epilepsy patients are shorter and have different content when compared to a control group. Moreover, epileptic patients' dreams feature higher proportions of familiar characters and settings, and lower proportions of success and sexuality. Interestingly, some differences were found based on the location of the epilepsy; patients with left TLE had higher dream recall frequency, more aggression, fewer animals, and more self-negative expressions compared with right TLE.[137]

Despite technological advances and growing theoretical interest in the study of dreams, few studies have investigated the relationship between dreams and epilepsy. Most studies focused on dream recall in epilepsy patients [131,138], and some also explored dream content.[131,137] The results of these studies implied that patients with epilepsy experience alterations in dream recall (i.e., decrease in DRF), possibly linked to alterations in REM sleep. Also, different in dream content, often related to negative themes with familiar setting were reported [137]. These findings highlight the fact that epilepsy affects cognition not only during wakefulness but also during sleep. Although the exact purpose of dreams is still unclear, there are many theories regarding their functional impact on emotional and cognitive states. Further studies that use advanced technologies could increase our understanding of the neurobiology of dreams, their biological and psychological influence and how these influence neurological patients.

2. Aim of the study

By the short introduction to the themes, it is clear that distinct pathological conditions can be associated with particular modification of frequency, structure or content of oneiric experience. In fact, available evidence shows that changes in dream features may reflect specific anatomic-functional alterations affecting brain areas that are involved in corresponding cognitive function. However, these changes not always correspond with similar changes in waking experience. They may also proceed or accompany the development of clinical symptoms manifested during the waking period.

Indeed, these observations imply that the analysis of dream experiences could provide unique information about the brain and mental health, which may serve as complement to the information obtained during the waking period.

The main goals of the present thesis project were to investigate the relation between dream content alteration in patients with focal epilepsy. And by that, deepen our knowledge regarding the neurophysiology of dreaming and in particular anatomic-functional mechanisms involved in the generation and delineation of dream imagery in physiological and pathological conditions. We hypothesized that dream content will differ between focal epilepsy patients and control group.

3. Materials and methods

3.1. Participants

A population of epilepsy patients was recruited at the Epilepsy Monitoring Unit (EMU) of the Baggiovara Civil Hospital (OCB) in Modena, starting from January 2024. The diagnosis was made by board-certified neurologists with expertise in epileptology and according to ILAE criteria[20] . All participants were native Italian speakers between the ages of 18 to 65 years old that have consented to participate in the study. For each patient who met the inclusion criteria, the following clinical variables were collected: age of first seizure, years of epilepsy duration, history of febrile seizures during childhood, the epileptogenic lobe, etiology, and number and type of ASMs intake. Patients were classified as drug-resistant or drug-responsive based on the ILAE criteria[50]. During the hospitalization, all the recruited patients underwent a long-term video EEG (LT-VEEG) monitoring, an MRI evaluation, and a complete neuropsychological assessment.

Finally, a population of healthy volunteers recruited at IMT School for Advanced Studies in Lucca and matched for age and sex to the patient's group was included in the study.

3.1.1. Dream study framework

For the study aims, patients and controls were evaluated using various sleep-related questionnaires and emotional state questionnaires. All participants were provided with an actigraph and a voice recorder (**Figure 3**). The actigraph is a wrist-worn device used to verify the regularity of sleep-wake patterns[139]. Participants were asked to record a dream report and a waking report each day for 14 days through a voice recorder. The specific instructions were: *"We ask you to register every morning what was going through your mind just before waking up. It could be a proper dream, or just an experience, like a picture or a sensation."*

For the purposes of the present thesis, we focused on questionnaires only.

Figure 3: actigraph (left) and a voice recorder (right)

3.1.2. Imaging acquisition

All patients underwent an MRI evaluation on a 3T scanner for clinical purposes. For the present study, the anatomical high-resolution 3D-T1 weighted sequences (3DT1) acquired at 1 mm slice thickness were collected. The imaging protocol followed the harmonized neuroimaging of epilepsy structural sequences (HARNESS) guidelines[140] , which are designed to recognize structural brain abnormalities in epilepsy patients.

Structural MRI was not available for one patient, and for the whole control population.

3.2. Assessments

3.2.1. Cognitive assessment

The cognitive assessment for the participant included the evaluation of the following functions: global cognition, executive, attention and processing speed, verbal memory, visual memory, visuospatial abilities, and language.

Mini-mental State Examination (MMSE) [141] was performed at an interview level to assess global cognitive performance[142]. MMSE is composed of 11 questions that evaluate 5 cognitive domains: orientation, registration, attention and calculation, recall, and language. The test has a maximum total score of 30 points; scores <23 are considered indicative of cognitive impairment.[143]

Stroop color/word interference test [144] is also known as "the color word naming test".[145] The test has been used to test the ability to block cognitive interference.[146] In this test, subjects are

asked to name the color of a work presented with a different ink color. [147] For the interpretation of the results are interpreted using reaction time and errors. The Italian version is provided by Caffara et al. (2002).[148]

Babcock Short Story Recall test is a verbal memory test that studies both immediate and delayed verbal memory [149] . The test is composed of two levels: (i) the examiner reads the story, and then asks for immediate recall, (ii) following a short time interval (e.g., 10 minutes), the examiner asks for delayed recall. The result consists of the sum of the immediate and the delayed recall.[150] The Italian version is provided by De Renzi et al. (1977).[151]

Rey-Osterrieth complex figure is a test used to evaluate visual and spatial ability, visual memory, and executive functions.[152] The subjects was asked to copy a complex geometric figure that contains 18 patterns in the most accurate way possible.[153] The test contains two components, one immediate copy and a delayed copy after 10 minutes. The immediate copied figure focuses on visual-constructional ability, while the delayed recall copy assesses long-term visual memory. The Italian version is provided by Bertolani et al. (1993).[154]

Verbal fluency test consists of two subtests: category fluency and letter fluency. Both of them explore language abilities. In the category fluency test, participants are instructed to name as many words as possible belonging to the same specific semantic group (i.e., colors, animals, fruits). In the letter fluency test, participants are asked to generate as many words as possible beginning with a specific letter (i.e., A, F, S). [150] The Italian version is provided by Costa et al. (2014).[155]

3.2.2 Questionnaires

Study participants have undergone a series of self-assessment inventories to evaluate their mental health state.

Beck's Depression Inventory is a self-report questionnaire that reflects the severity of depression. It evaluates attitude and symptoms of depression[156] through 13 items and multiple choice questions. Every item contains a manifestation of depression, and the participant rates the item on a scale from 0 to 4. Higher scores indicate higher depression grade.[157] In our study, the Beck's depression inventory was available for patient group only.

State-Trait Anxiety Inventory for Adults (STAI) is a self-assessment questionnaire that evaluates anxiety. [158] In our study, we used the STAI-Y2 version that measure trait anxiety.[159] The test consists of 20 assertions that ask the participants to describe how they feel during everyday life. They are required to respond indicating on a 1 to 4 scale the frequency of anxiety symptoms.[160] The scoring method involves adding items to obtain a total score. For anxiety absent items (i.e., 1, 3, 6, 7, 10, 13, 14, 16, and 19), scoring should be reversed.[161] The range of scores goes from 20 to 80, with higher scores indicating a higher anxiety trait.[161] Some traits has been grouped together to highlight a specific area of anxiety, such as: cognitive concern (item 16), tension and restlessness (item 7,13), low self-esteem or sense of inadequacy (item 3), low calmness and general well-being (item 1,6,10,14,19).

Subsequentially, every enrolled participant filled out a series of questionnaires aimed to investigate their sleep quality, dream recall, and their mental imagery during wakefulness.

Attitude towards dreaming questionnaire[162] studies the individual's positive and negative views towards dreaming. [163] The test presents a series of 6 affirmations that the participant needs to rate on their level of Agreeableness. The affirmation studies the subject's mindset towards dreaming. For the results interpretation, higher scores are associated with a more positive attitude toward dreams.[164]

Morning dream recall[165] contains a series of questions that review the frequency of dream recall (i.e., the ability to remember a dream while awake), and some aspects of dream content. Dream recall frequency is measured on a 7 points scale. Additionally, several items were developed to assess a qualitative aspect of dreams, including realism in dreams (3 point scale), creative aspects of dreams (5 point scale), emotional intensity (5 point scale), emotional tone of dreams (scale range: from -1=predominantly negative, 0=balanced, +1=predominantly positive). The version was adapted from Schredl et al (2002)[165].

The Epworth sleeping scale is a test that measures the subject's general level of daytime sleepiness.[166] The participant are asked to answer 8 affirmations that describe different situations in which they can fall asleep. The total score can range between 0 to 24, the higher the *Epworth sleeping scale* is, the higher the person's daytime sleepiness is.[167]

Mind wandering spontaneous scale [168] contains 8 affirmations that regard the person's thoughts and mind wandering. The questions are divided into two categories: spontaneous (MW-S) and deliberate (MW-D) mind wandering. For each category, there are 4 questions.[169] Both

categories are scored using a 7-point scale system for each affirmation[168]. The results reflect the individual's tendency toward mind wandering; the higher the score, the greater the inclination for mind wandering.

Pittsburgh Sleep Quality Index (PSQI), developed by Buysse et al. (1989), is a standardized questionnaire designed to assess sleep quality.[170] The test contains 19 self-rated questions and 5 rated by a bedpartner or roommate.[170] In our study, only the self-rated questions were used. The 19 questions are used to assess a variety of elements regarding sleep quality, including estimating sleep duration, latency, and any sleep-related problems. The items are grouped into seven component scores, each weighed on a 0-3 scale. The 7 components are then summed to a global PSQI score, ranging from 0-24, with higher scores indicating worse sleep quality.

Vividness of Visual Imagery is a questionnaire used to analyze visual mental image vividness.[171] The questionnaire contains 16 items, divided into 4 groups with 4 items each. For each item the participant is asked to summand an image, and then to rate it from 1 to 5 based on the vividness of the image.[172] The score is summed, ranging from 16 to 80, a higher score indicates more vivid visual imagery.

The Horne-Östberg Morningness Eveningness Questionnaire evaluates the difference in circadian rhythm between individuals. [173] Consists of 19 items, the items are composed of both Likert-type and time scale questions.[174] To obtain a global score the items are summed and then the total score is converted to a 5 point scale: definitely morning type (scoring 70-86), moderately morning type (scoring 59-69), neither type (scoring 42-58), moderately evening type (scoring 31-41), and evening type (scoring 16-30).[174]

3.3. Statistical analysis

All the following statistical analyses were made with IBM SPSS software, a statistical software used for data analysis.[175]

Demographic and clinical variables were reported as means and standard deviations (SD). Differences between patients and controls in age and education were assessed using Independent Samples t-tests. While the Chi-square test was used to analyze to difference in sex distribution between the two groups. Likewise, neuropsychological performances and

questionnaire scores were compared between patients and controls with Independent Samples t-tests. Statistical significance for all tests was set at $p<.05$.

3.3.2. MRI pre-processing

Cortical thickness and subcortical volumes were obtained from the 3DT1 sequences using FreeSurfer (v7.3.2) software[176]. 3DT1 sequences were parcelled in 68 cortical regions of interest (ROIs), and cortical thickness was derived based on the Desikan-Killiany atlas.[177] Subcortical segmentation was performed using FreeSurfer's automated pipeline, yielding volumetric estimates for 16 subcortical structures. A dedicated FreeSurfer pipeline was also employed to subsegment the hippocampal subfields[178] and amygdala nuclei[179]. The following hippocampal subfield volumes were extracted for each hemisphere: hippocampal body, hippocampal head, hippocampal tail, and whole hippocampal volume. As shown in **figure 4**[180], the amygdala segmentation identified nine nuclei per hemisphere: anterior amygdaloid area (AAA), cortico-amygdaloid transition area (CAT), basal nucleus (Ba), lateral nucleus (La), accessory basal nucleus (AB), central nucleus (Ce), cortical nucleus (Co), medial nucleus (Me), and paralaminar nucleus (PL). As previously described[181–184], the amygdala subnuclei were clustered based on cytoarchitecture, histochemical properties, and connectivity patterns[185,186] into three major complexes: *(i)* the basolateral amygdala (BLA) is the deepest complex, which includes La, Ba, AB and PL nuclei; *(ii)* the superficial group is named cortical amygdala (CA), and is composed by the Co nucleus only; *(iii)* finally, the central-medial amygdala (CMA) is

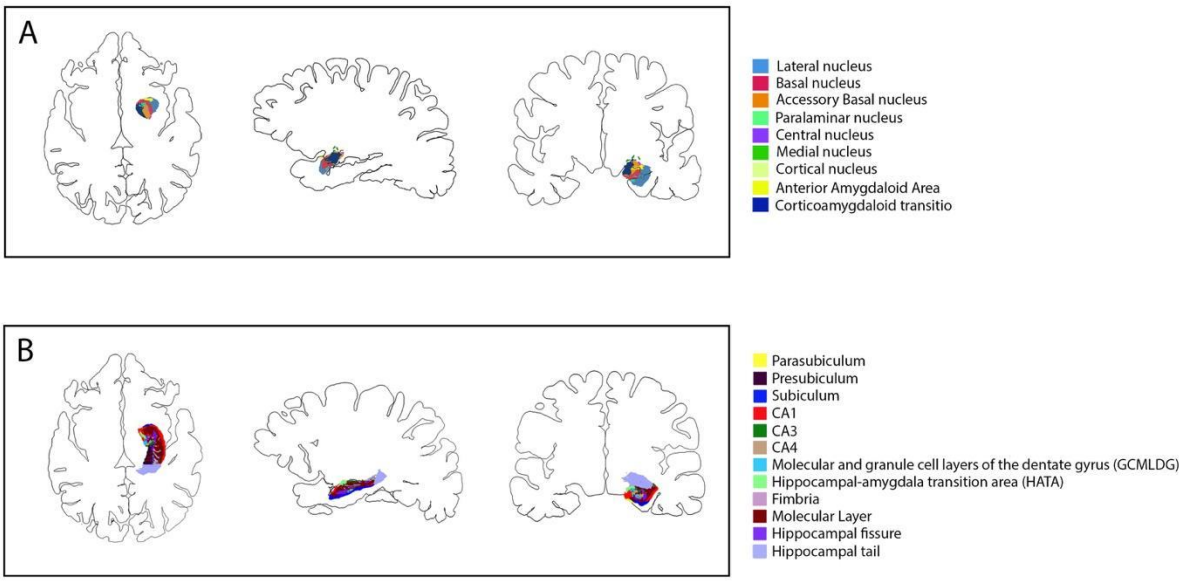

Figure 4: A. Amygdala parcellation into nine subnuclei. B. Hippocampal subfields segmentation

composed of the Me and Ce nuclei. Visual inspection of morphometric segmentations was performed following the standardized FreeSurfer protocol and according to ENIGMA standardized protocols (http://enigma.usc.edu).

3.3.3. Brain morphometry analysis and correlations

All cortico-subcortical ROIs were converted to z-scores. To account for the lateralization of the epileptogenic zone (EZ), brain features from right-sided patients were flipped, in order to have all the morphometric data on the left side. Therefore, all morphometric values and results were reported as ipsilateral and contralateral relative to the EZ. From the 68 cortical regions, we selected the bilateral entorhinal cortex, the parahippocampal gyrus (PHC), and the temporal pole as cortical thickness measures (mm^2) (**figure 5**). Moreover, a composite score named "medial temporal lobe" was obtained by averaging the mentioned ROIs. As far as the subcortical ROIs, bilateral hippocampal and amygdalae volumes, as well as their subnuclei volumes, were collected.

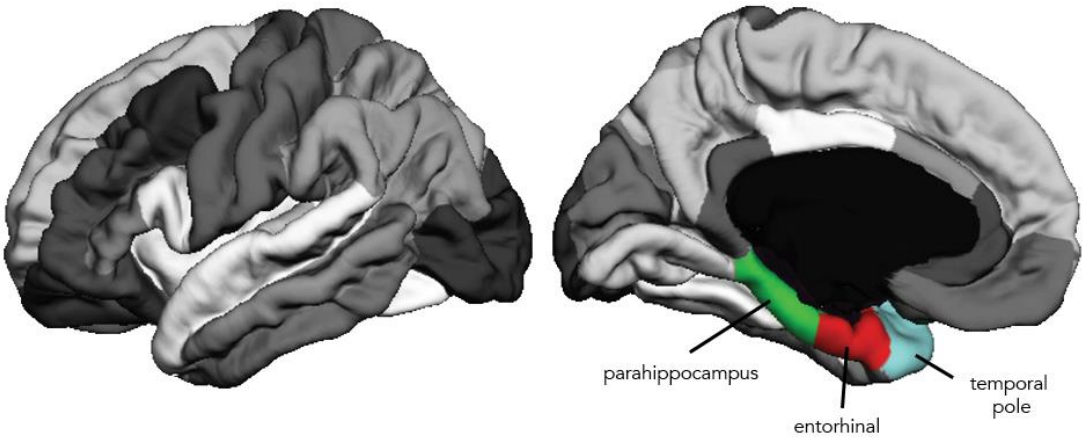

Figure 5: segmentation of parahippocampal cortex, entorhinal cortex and temporal lobe as represented in the Dasikan atlas

Then, we performed Pearson's correlations between the selected cortico-subcortical features and questionnaire scores. The correlations were performed within the whole patients group. Subsequently, the correlation analysis was repeated exclusively on 14 patients diagnosed with TLE. Statistical significance for all tests was set at $p<.05$.

4. Results

4.1. Clinical features

The clinical group consisted of 19 patients diagnosed with epilepsy who were recruited to the study from February 2024 to January 2025. The patient group included 9 males (47.37%) and 10 females (52.63%), with a mean age of 37.84 (±12.47, range 19-63) years. All patients were diagnosed with focal epilepsy; 15 (78.94%) with temporal lobe epileptic localization (6 right lateralized and 9 left lateralized), and frontal lobe epilepsy was identified in 4 (21%) patients (1 with right-sided localization and 3 with left-sided localization).

Thirteen patients (68.42%) have been identified with a structural etiology, while 6 patients (31.57%) were referred to as “indeterminable”. Within the first group, the cause for structural abnormalities were classified as 7 FCD, 1 patient had Encephalocele, 2 patients had Cerebral Cavernous Malformation (CCM), and 3 patients had suspected or confirmed brain neoformation.

Eighteen patients (94.74%) are currently being treated with ASMs: 6 with only one drug, 6 with 2 drugs combined, 3 with 3 drugs combined, and only 1 with 4 drugs combined. Only 3 patients were identified with drug-resistant epilepsy.

Finally, only 2 patients had undergone neurosurgical treatment: one received an anterior cingulotomy, while the other underwent resection of the anterior epileptogenic zone.

4.2. Demographic characteristics

Patients and controls were compared for demographic characteristics, and results are summarized in Table 1. There were no significant differences in age and gender between patients and controls. However, patients showed lower education when compared to controls (t=-2.275, p=.030).

	Patients	Controls	Stat.	Sign.
N	19	15		
Age (y)	37.84(±12.580)	38.47(±13.695)	-.138^{t}	.891
Sex (F/M)	10/9	6/9	.537^{x2}	.464
Education (y)	12.47(±3.672)	14.93(±2.251)	-2.275^{t}	**.030**

Table 1. Clinical comparison between patients and controls. *Age and education are presented as mean (± standard deviation). Age and education are expressed as years (y). Sex is represented as "female" (F) and "male" (M). t: Independent-sample t-test, χ^2: chi-squared test. Sign: p-value.*

4.3. Cognitive assessment results

Cognitive assessment revealed lower MMSE scores in patients with respect to controls (t=-4.548, p=.000), as well as in the Rey-Osterrieth complex figure immediate copy (t=-2.621, p=.014), while no differences were found in the delayed copy. Moreover, patients showed lower scores in the category fluency (t=-4.618, p=.000), and in the letter fluency (t=-3,472, p=.002). The cognitive assessment did not reveal any other differences between patients and controls; results are summarized in Table 2.

	Patients	Controls	Stat.	Sign.
MMSE	26.20(±1.976)	28.90(±1.290)	-4.548[t]	**.000**
STROOP time	20.62(±5.811)	18.47(±7.421)	.862[t]	.396
STROOP error	0.70(±.932)	0.31(±.728)	1.282[t]	.210
Babcock Short Story Recall	16.45(±7.490)	16.82(±3.609)	-.170[t]	.866
Rey-Osterrieth complex figure (immediate)	32.70(±2.309)	34.83(±2.056)	-2.621[t]	**.014**
Rey-Osterrieth complex figure (delayed)	18.24(±5.455)	20.30(±4.724)	-1.087[t]	.287
Category fluency	40.58(±11.433)	55.29(±11.383)	-3.472[t]	**.002**
Letter fluency	26.90(±6.724)	39.61(±7.984)	-4.618[t]	**.000**

Table 2. Cognitive assessment is compared between patients and controls. *All tests are presented as mean (± standard deviation). MMSE: mini mental state examination, STROOP: Stroop color/word interference test reaction time and error. t: Independent-sample t-test. Sign: p-value.*

4.4. Questionnaires results

When STAI-Y2 total scores were evaluated, no differences were found in trait anxiety between patients and controls. However, a statistical significance difference was found in item 19 *"I feel calm"*, where patients showed lower scores compared to controls. This is one of the positive affirmations so the score, so it needs to be inverted, meaning that a lower score indicates that patients tend to agree more with the statement. (t=-2.077, p=.046). All results of STAI-Y2 are summarized in Table 3.

As far as Beck's Depression Inventory, scores were available only in the patient group, the mean score was 2.79(±2.097).

	Patients	Controls	Stat.	Sign.
STAI-Y2 total	39.05 (±10.559)	38.93 (±8.787)	.035[t]	.972
Tension and restlessness	5.84 (±1.385)	5.60 (±1.183)	.539[t]	.594
Low calmness & well-being	10.16 (±2.566)	11.00 (±2.699)	-.929[t]	.360

Item 3	2.16 (±.958)	2.20 (±.414)	-.159[t]	.875
Item 16	1.79 (±.631)	1.93 (±1.93)	-.678[t]	.503
Item 19	1.84 (±.898)	2.47 (±.834)	-2.077[t]	**.046**

***Table 3**: STAI-Y2 questionnaire scores between patients and controls. All scores are presented as mean (± standard deviation). Tension and restlessness are expressed as the sum of items 7 and 13, while low calmness and general well-being is the sum of items 1, 6, 10, 14, and 19. STAI: Questionary State-Trait Anxiety Inventory for Adults, t: Independent-sample t-test, Sign: p-value.*

Table 4 shows dream-related questionnaire results. We reported a statistical significant difference in the spontaneous category of the Mind wandering spontaneous scale, with patients showing lower scores compared to controls (t=-2.581, p=.015). The deliberate category of the same scale was not found different, nor were the other dream-related questionnaires.

	Patients	**Controls**	**Stat.**	**Sign.**
PSQI	5.58 (±2.714)	4.87 (±2.264)	.816[t]	.421
ESS	6.21 (±2.898)	4.87 (±3.502)	1.225[t]	.230
MEQ	55.05 (±9.040)	54.33 (±8.372)	.238[t]	.813
VVQ	58.53 (±11.621)	62.33 (±12.034)	-.934[t]	.357
MWS-S	10.74 (±4.357)	14.33 (±3.579)	-2.581[t]	**.015**
MWS-D	12.05 (±4.882)	14.47 (±5.780)	-1.320[t]	.196
ATD	8.89 (±2.132)	9.47 (±3.603)	-.577[t]	.568

Table 4: Dream-related questionnaire scores between patients and controls. *All tests are presented as mean (± standard deviation). PSQI: Pittsburgh Sleep Quality Index (total score), ESS: The Epworth sleeping scale (total score), MEQ: The Horne-Östberg Morningness Eveningness Questionnaire (total score), VVQ: Vividness of Visual Imagery (total score), MWS-S: Mind Wandering Spontaneous Scale spontaneous category (total score), MWS-D: Mind Wandering Spontaneous Scale deliberate category (total score), ATD: Attitude towards dreaming (total score). t: Independent-sample t-test. Sign: p-value.*

	Patients	**Controls**	**Stat.**	**Sign.**
Frequency	3.79 (±1.357)	4.20 (±.941)	-.996[t]	.327
Memory	2.37 (±.831)	2.53 (±.516)	-.672[t]	.506
Richness	1.95 (±.780)	2.20 (±1.014)	-.822[t]	.417
Thought-Like	.89 (±.567)	1.00 (±.926)	-.409[t]	.685
Vividness	2.58 (±.692)	2.13 (±.640)	1.926[t]	.063
Bizarre	1.79 (±.855)	2.00 (±1.069)	-.639[t]	.528
Awareness	2.05 (±1.177)	2.00 (±.756)	.150[t]	.882
Lucidity	1.37 (±1.165)	1.13 (±.743)	.679[t]	.502
Nightmares	1.00 (±.745)	1.47 (±1.246)	-1.357[t]	.184
Repetitive	.47 (±.513)	.93 (±1.033)	-1.697[t]	.099
Exhausting	.95 (±.705)	1.20 (±1.014)	-.856[t]	.398
Persistence	1.58 (±1.017)	1.80 (±1.082)	-.612[t]	.545
Environment	1.11 (±1.487)	1.40 (±1.805)	-.522[t]	.605
Consciousness	-.42 (±.692)	-.07 (±1.223)	-1.067[t]	.294
Emotion Valence	.53 (±.612)	-.07 (±.961)	2.190[t]	**.036**
Emotion Strength	1.89 (±.315)	2.07 (±.704)	-.953[t]	.348
Aggression	.74 (±.806)	1.20 (±.775)	-1.693[t]	.100

Risk	.84 (±.958)	1.27 (±.799)	-1.378[t]	.178
Visual	2.63 (±1.065)	2.73 (±1.223)	-.259[t]	.797
Tactile	1.53 (±.964)	1.40 (±.986)	.376[t]	.710
Auditory	2.16 (±.958)	1.67 (±1.047)	1.425[t]	.164
Other senses	.95 (±1.079)	.67 (±.900)	.809[t]	.424

Table 5: Morning Dream Recall questionnaire scores between patients and controls. *All answers regarding dream content are presented as mean (± standard deviation). The 22 elements presented in the questionnaire: Frequency, Memory, Richness, Thought-Like, Vividness, Bizarre, Awareness, Lucidity, Nightmares, Repetitive, Exhausting, Persistence, Environment, Consciousness, Emotion Valence, Emotion Strength, Aggression, Risk, Visual, Tactile, Auditory, Other senses. t: Independent-sample t-test. Sign: p-value.*

Table 5 reports analyses of the Morning Dream Recall questionnaire, which consists of 22 items. The results showed higher "Emotional Valence" in patients' dreams compared to controls (t=2.190 p=.036). None of the other item reached statistical significance.

4.5. MRI data results

Correlation analysis was performed between selected cortical regions and questionnaire items that reached statistical significance.

Our results showed a negative correlation between STAI questionnaire item 19 and the ipsilateral amygdala. Specifically, with the Ba (r=-.507, p=.032), the AB (r=-.531, p=.024), PL (r=-.552, p=.017), and the whole BLA (r=-.506, p=.032), as well as with the CAT (r=-.552, p=.018).

The "Emotional valence" from the Morning Dream Recall questionnaire, showed a positive correlation with the ipsilateral temporal pole (r=.550, p=.018) and with few contralateral regions; including the PHC (r=.520, p=.027), temporal pole (r=.650, p=.003), and the whole medial temporal lobe (MTL) (r=.003, p=.011).

Finally, a negative correlation was found between the MWS-S and the ipsilateral entorhinal cortex, as illustrated in **figure 6** (r=-.521, p=.027), and between the MWS-S and the

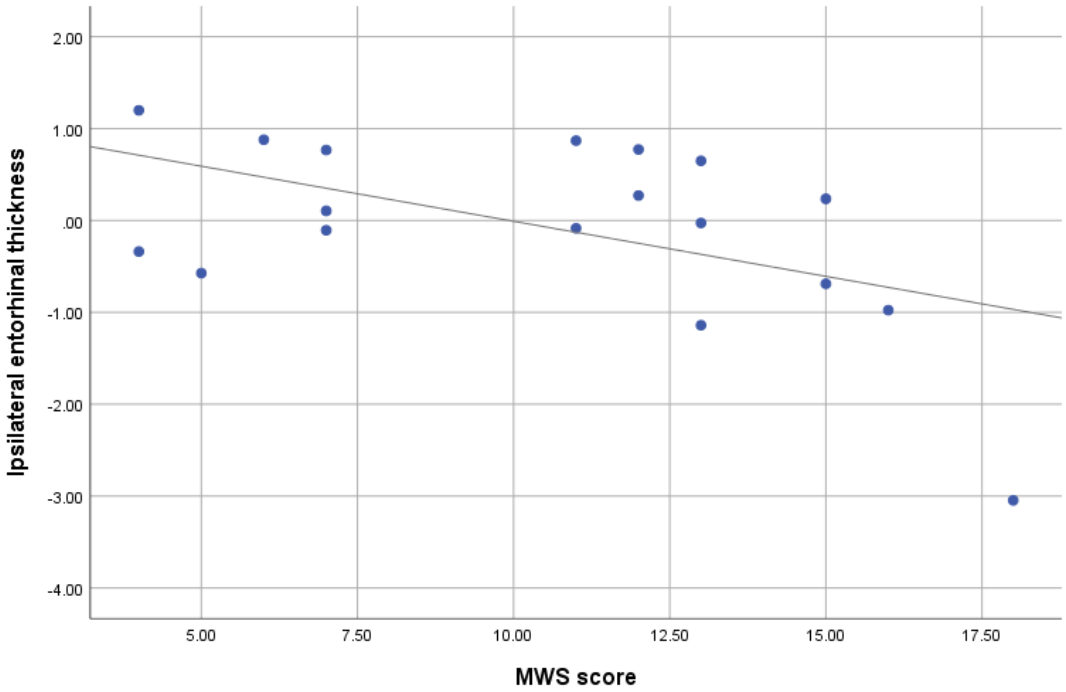

Figure 6: the graph displays the relationship between ipsilateral entorhinal average thickness, expressed in Z-score (variable Y) and MWS scale score (variable X)

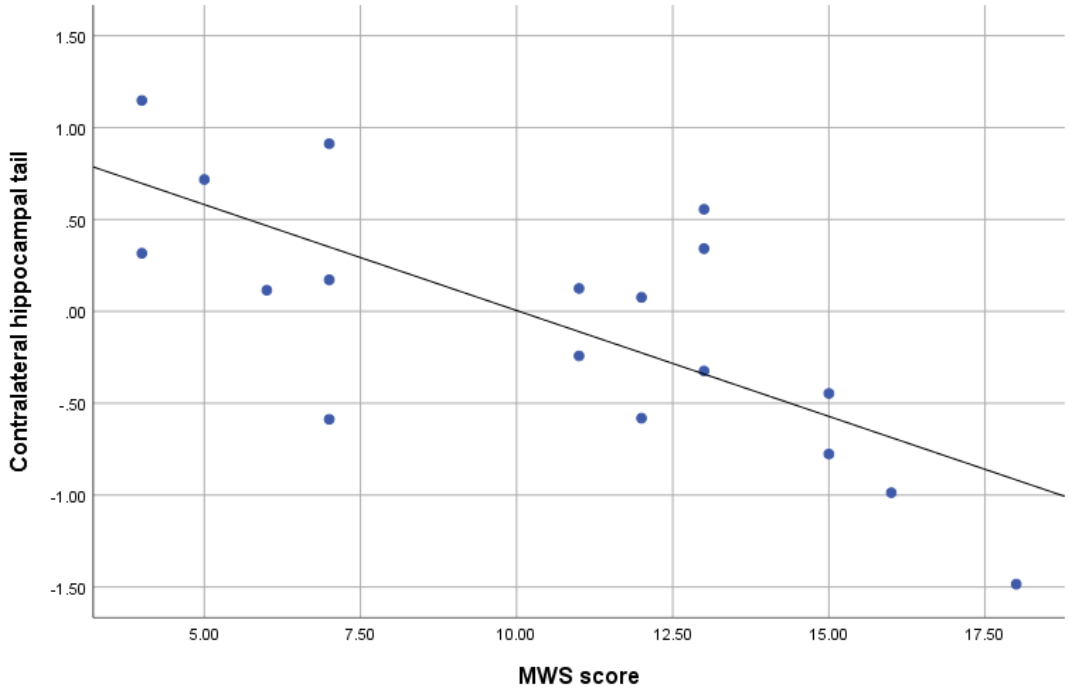

Figure 7: the graph displays the relationship between contralateral hippocampal tail volume, expressed in Z-score (variable Y) and MWS scale score (variable X)

contralateral hippocampal tail, as displayed in **figure 7** (r=-.730, p=.001). As for the amygdala, a correlation was between the MWS-S score and the contralateral Ce (r=-.484, p=.042).

When focusing on the TLE group only, additional new correlations were observed. In TLE population, STAI item 19 was related the whole ipsilateral amygdala volume (r=-.554, p=.040) and to several ipsilateral subnuclei: the Ba (r=-.617, p=.019), CAT (r=-.646, p=0,013), PL (r=-.673, p=.008), and BLA (r=-.603, p=.023), and the AB (r=-.581, p=.029).
As for the item "emotional valence", we confirmed the involved of bilateral temporal poles [ipsilateral: (r=.622, p=.018), contralateral: (r=.676, p=.008)], however, some previously observed associations were no longer presenting, including the associations with the PHC and MTL.

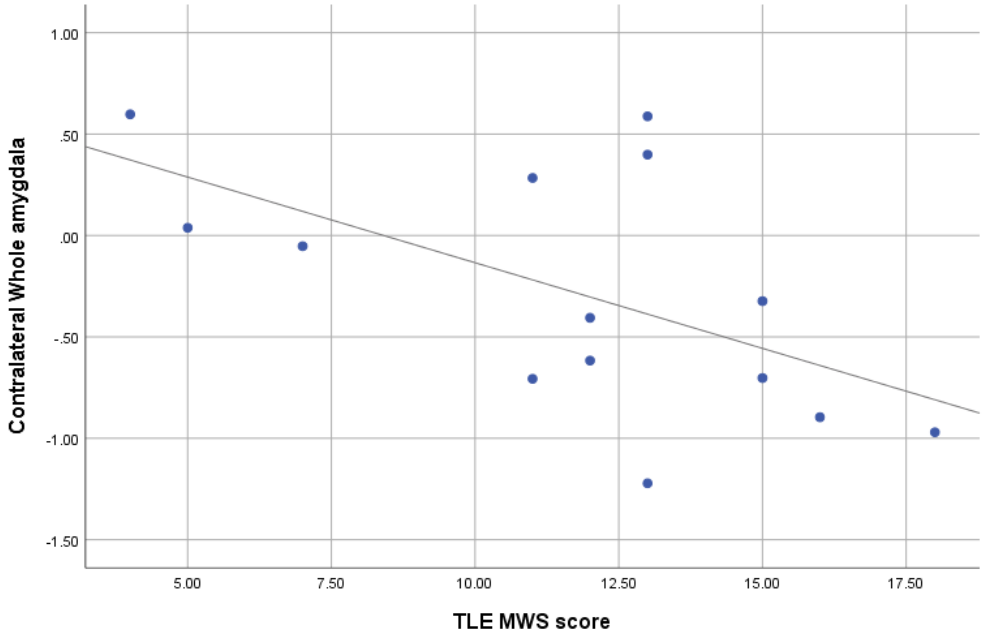

Figure 8: the graph present the relationship between controlaterasl whole amygdala, expressed in Z-score (Y varibale) and MWS score in TLE patients (X variable)

Regarding the MWS-S, new correlation was revealed, particularly in contralateral regions, including the whole hippocampal volume (r=-.554, p=.04) and the whole amygdala volume as represented in **figure 8** (r= -.568, p=.034). Moreover, some amygdala subnuclei were associated with MWS-S as well; AB, as shown in **figure 9** (r=-.568, p=.034), Me (r=-.537, p=.048), and the BLA (r=-.541, p=.046). We also confirmed the involvement of the ipsilateral

entorhinal cortex (r=-.553, p=.04), the contralateral Ce (r=-.673, p=.008), and the contralateral hippocampal tail (r=-.784, p=.001).

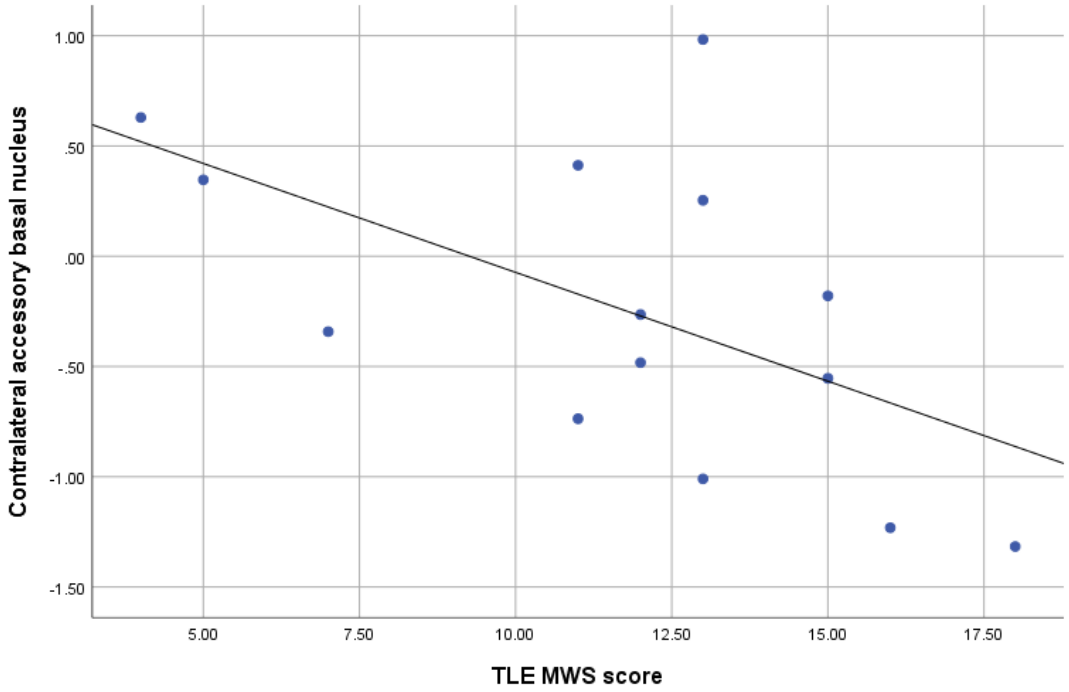

Figure 9: the graph presents the relationship between contralateral accessory basal nucleus, expressed as Z-score (variable Y) and MWS score in TLE patients (variable Y)

5. Discussion

The present study aimed to explore the difference in dream content between focal epilepsy patients and healthy controls, by using both behavioral and imaging data. Important differences were found between patients and controls across demographic, cognitive assessment, and self-reported questionnaire measures. Additionally, structural MRI analysis revealed association between certain brain areas volume and high score in selected item and scale from the questionnaires.

Significant difference was revealed in education level, and neuropsychological assessments. Particularly, on the MMSE, the immediate copy of Rey-Osterrieth complex figure, and category and letter fluency tests, with patients performing significantly worse. These findings are consistent with existing literature, which has shown that patients with epilepsy are more inclined to cognitive and behavioral deficits.[187]

In the questionaries segment of the data, a relevant statistical difference was found in trait 19 of the STAI questionnaire, presenting a lower mean in patients group. Because trait 19 is one of the positive affirmations (e.g., "I feel calm"), the score needs to be inverted, so a lower score in this trait actually indicates that patients tend to agree more with the statement. This finding is unexpected, given that epilepsy has been associated with anxiety and stress, not only as a consequence of the disease but also as a cause of disease progression.[188]

The item "emotional valence" has proven statistically significant difference between patients and controls. This indicates that patients have a more positive emotional valence to their dreams in comparison to controls. Previous study by Ciuffini et al. (2018), has demonstrated that patients with temporal mesial lobe epilepsy have a higher mean valence when rating neutral and socially pleasant pictures.[189] Thus, epilepsy in some cases can be associated with higher emotional reactivity. An alternative explanation may relate to a difference in dream recall. It has been seen that epilepsy is associated with lower dream recall[190], so we can assume that all dream experiences, rather positive or negative, are less likely to be remembered by the subject, so the overall emotional valence of dreams can remain positive. However, this theory was challenged by Solms[191], who suggests a link between nightmares and nocturnal ictal activity. On the other hand, the DRQ "Nightmares" item presented a lower mean in the patients group in comparison to controls, suggesting that patients experience negative dream content less

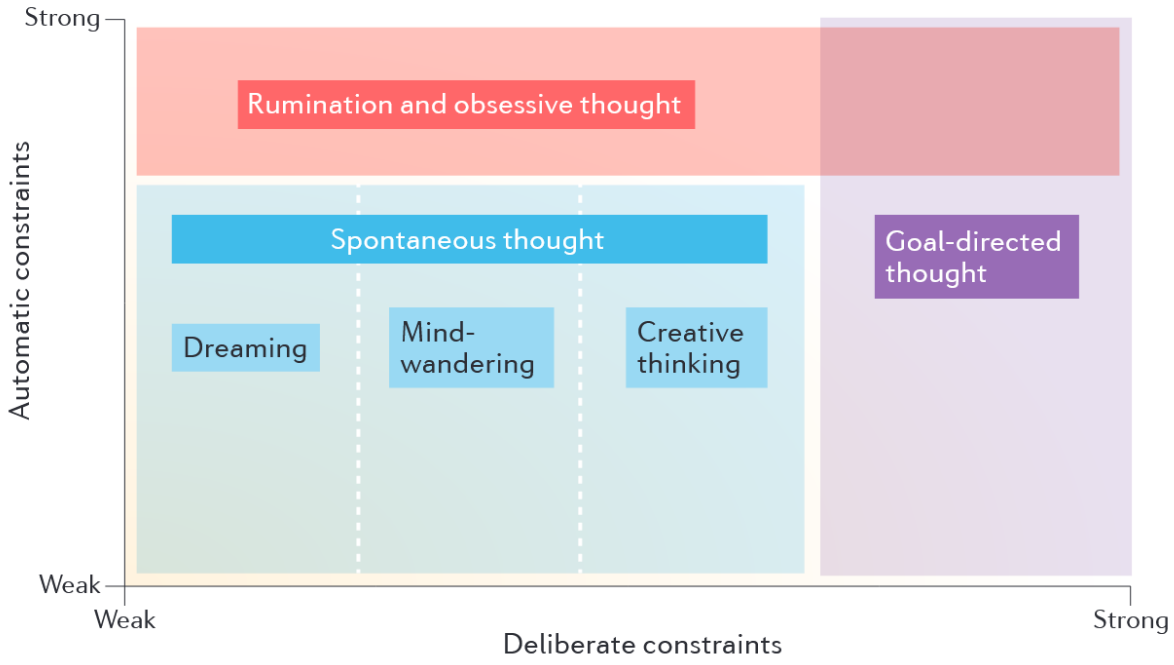

Figure 10: Conceptual space relating different types of thought

frequently. However, it did not reach a statistical significance and therefore should be interpreted with caution.

The MWS-S resulted significantly lower in patients than in controls, suggesting that patients tend to engage less in spontaneous mind wandering. To better interpret this finding, a deeper understanding of the concept of mind wandering is necessary. Recent literature conceptualized mind wandering as form of spontaneous thought, more structured than dreaming, yet less than creative thinking and goal-directed thought.[192,193] As shown in **Figure 10**[192], spontaneous thought can be seen as a spectrum, with dreaming representing the most unconstrained and immersive form. Dreaming is considered a type of spontaneous thought that is highly unconstrained, hyperassociative, and deeply engaging.[192] Given this framework, the reduced frequency of mind wandering observed in patients with focal epilepsy may reflect a broader alteration in their capacity of spontaneous thought. This may be extended to a lower capacity of dreaming, or an alteration in the subjective nature and quality of dream experience.

5.1. STAI and amygdala volume

The amygdala is a core of subcortical regions that participate in affective and motivation-related behavior. [194] Neurological research has identified the amygdala as a central component in the processing of threat.[195] Certain types of anxiety have been associated with dysregulation of the brain's network of fear, including the amygdala, hippocampus, insula, anterior cingulate, and prefrontal cortex (PFC). [196]

In our study, trait 19 of the STAI questionnaire resulted negatively associated with ipsilateral amygdala subnuclei volumes, including: the Ba, AB, CAT, PL, and BLA. Showing higher scores on trait 19 were associated with lower volume in these subregions. These results are consistent with the literature, which indicates that individuals with anxiety disorders have significantly smaller amygdala.[196,197] Moreover, a reduced volume of specific regiones of the amygdala, in particular the BLA, may reflect alteration in threat regulation. Yang et al. (2018) studied variations in amygdala volumes in mouse, have demonstrated that a small BLA volume is associated with enhanced fear conditioning and exaggerated stress-associated response.[198] In patients with TLE, results demonstrated even stronger correlation, suggesting an association between EZ and alteration in amygdala subregions.

5.2. Emotional valence and medial temporal lobe

The item "emotional valence" from the DRQ questionnaire was positively correlated with subregions found in the medial temporal lobe. On the ipsilateral side, correlation was made with the temporal pole thickness. On the contralateral side, correlation was found with parahippocampal thickness, temporal pole thickness, and the MTL. These results suggest that positive valence in dreams is associated with greater volumes of these subregions among patients with focal epilepsy. In recent articles, these areas were associated with various cognitive and affective functions. In particular, the temporal pole was associated with socio-emotional processing among numerous other functions.[199] The MTL is highly interconnected with the amygdala, enhancing the processing of emotional memories.[200] The parahippocampal gyrus has been associated with many cognitive processes, including episodic memory and visuospatial abilities;[201] furthermore, it has a role in the processing of emotional stimuli.[202]

Therefore, an increased volume in areas that are involved in emotional processing, especially the processing of emotional memory, seems to correlate with positive emotional dream valence. These results suggest a potential neurological basis linking dream and emotional memory systems.

Notably, the correlation was stronger on the contralateral side of the brain, and thus is less likely to be associated with EZ. Among patients with TLE, associations were similar, reinforcing the hypothesis that these findings are independent of the EZ.

5.3. MW-S correlation with amygdala and hippocampal

As previously mentioned, the cognitive process of spontaneous mind wandering is a part of the family of spontaneous thought that also includes creative thought and dreaming.[192] The neurological basis of this phenomenon are rooted in the default mode network (DMN) [203]. Within DMN, the medial temporal subsystem (DMN_{MTL}) is clustered around the MTL, and plays a central role in the constructive mental stimulations.[204] This subsystem contains the hippocampal formation, the PHC, and also includes a number of MTL cortical projections.[192] In our study, a negative correlation was found between MW-S and the cortical thickness in the ipsilateral entorhinal cortex. As for the contralateral side of the brain, correlation was made with the hippocampal tail and Ce of the amygdala. Suggesting that higher scores in the MW-S scale are associated with lower cortical thickness or volume in these specific subregions.

Among TLE patients new correlation emerges, including various nuclei of the contralateral amygdala. Such as BA, Me, BLA, and whole amygdala volume. These findings suggest that a higher MW-S score is associated with lower volume in this subregion. This association is unexpected, as the amygdala is typically described in the context of emotional processing, decision making, and motivational behavior.[205] However, Fox et al. (2018) suggest that spontaneous thought, in particular emotion-based thought, can be associated with the recruitment of the amygdala, among other emotional processing centers.[206] The correlation also concentrates on the contralateral side, so its likely EZ independent phenomena, indicating a brother correlation, perhaps a trait-like, between neuronal differences and spontaneous thought.

6. Limitations of the study

Despite our effort, this study presents several limitations that must be addressed. First, mental health questionnaires were not completed in the control group, with *Beck's Depression Inventory* completed only in the patients' group. While the majority of patients have been evaluated with an MRI scan, the control group was not, and therefore we could not elaborate the analysis of the difference between the groups and selected areas. Second, the sample size included for this thesis is relatively small, and this may explain the lack of statistical significance in questionnaires between groups, as most of the results have demonstrated differences in mean between the two groups, but did not reach statistical significance. Lastly, in our study, we only used self-reported questionnaires, a very common and standardized method, but one that carries the risk of limited accuracy. Future development of the present study will include a larger sample for both groups and a sophisticated artificial intelligence, which will elaborate the dreams registrations, recorded by participant during the study. In this framework, dreams content will be analyzed by other objective means.

7. Conclusions

Our study confirms that focal epilepsy patients experience differences in oneiric content in comparison to healthy controls. The results suggest alterations in cognitive processes such as emotional elaboration and spontaneous thought, which may influence dream experience in these patients. Specifically, patients with focal epilepsy appear to experience reduced cognitive activation during dreaming. Additionally, we confirmed a neurological basis for these alterations, localized in the medial temporal lobe, particularly involving several nuclei in the

amygdala and subregions of the hippocampus. This notion contributes to our understanding of the neurological processes underlying the operation of dreaming and explores the cognitive function it reflects. Furthermore, this alteration in dream content may be used as a valuable tool in the study of epilepsy, both as a method of evaluation of patients' cognitive function and the level of impermeant, and as a potential diagnostic marker, used to recognize patients with neurological disorders.

8. References

1. Guerreiro CAM. Epilepsy: Is there hope? *Indian J Med Res*. 2016;144(5):657. doi:10.4103/ijmr.IJMR_1051_16

2. Manford M. Recent advances in epilepsy. *J Neurol*. 2017;264(8):1811. doi:10.1007/s00415-017-8394-2

3. Seizures - Symptoms and causes. Mayo Clinic. Accessed November 25, 2024. https://www.mayoclinic.org/diseases-conditions/seizure/symptoms-causes/syc-20365711

4. Zuberi SM, Wirrell E, Yozawitz E, et al. ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: Position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022;63(6):1349-1397. doi:10.1111/epi.17239

5. Beghi E, Giussani G, Sander JW. The natural history and prognosis of epilepsy. *Epileptic Disord*. 2015;17(3):243-253. doi:10.1684/epd.2015.0751

6. Murray CJL, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*. 2012;380(9859):2197-2223. doi:10.1016/S0140-6736(12)61689-4

7. Beghi E, Giussani G, Nichols E, et al. Global, regional, and national burden of epilepsy, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*. 2019;18(4):357-375. doi:10.1016/S1474-4422(18)30454-X

8. Megiddo I, Colson A, Chisholm D, Dua T, Nandi A, Laxminarayan R. Health and economic benefits of public financing of epilepsy treatment in India: An agent-based simulation model. *Epilepsia*. 2016;57(3):464-474. doi:10.1111/epi.13294

9. guerrini2006.

10. Tian N. Active Epilepsy and Seizure Control in Adults — United States, 2013 and 2015. *MMWR Morb Mortal Wkly Rep*. 2018;67. doi:10.15585/mmwr.mm6715a1

11. Cascino G, Sirven JI, Tatum WO, eds. *Epilepsy*. Second edition. John Wiley & Sons, Inc; 2021. doi:10.1002/9781119431893

12. Forsgren L, Beghi E, Õun A, Sillanpää M. The epidemiology of epilepsy in Europe – a systematic review. *Eur J Neurol*. 2005;12(4):245-253. doi:10.1111/j.1468-1331.2004.00992.x

13. Helmstaedter C, Witt JA. Epilepsy and cognition - A bidirectional relationship? *Seizure*. 2017;49:83-89. doi:10.1016/j.seizure.2017.02.017

14. Shen B, Shi Y, Fu Y, Cao Y, Wang Y, Fang J. Deep brain stimulation on cognition in epilepsy: A concentration on learning and memory. *Brain Res Bull*. 2024;219:111134. doi:10.1016/j.brainresbull.2024.111134

15. Seidenberg M, Pulsipher DT, Hermann B. Association of Epilepsy and Comorbid Conditions. *Future Neurol*. 2009;4(5):663-668. doi:10.2217/fnl.09.32

16. Tellez-Zenteno JF, Patten SB, Jetté N, Williams J, Wiebe S. Psychiatric Comorbidity in Epilepsy: A Population-Based Analysis. *Epilepsia*. 2007;48(12):2336-2344. doi:10.1111/j.1528-1167.2007.01222.x

17. Sillanpää M, Shinnar S. SUDEP and other causes of mortality in childhood-onset epilepsy. *Epilepsy Behav*. 2013;28(2):249-255. doi:10.1016/j.yebeh.2013.04.016

18. Beniczky S, Trinka E, Wirrell E, et al. Updated classification of epileptic seizures: Position paper of the International League Against Epilepsy. *Epilepsia*. n/a(n/a). doi:10.1111/epi.18338

19. Fisher RS, Cross JH, D'Souza C, et al. Instruction manual for the ILAE 2017 operational classification of seizure types. *Epilepsia*. 2017;58(4):531-542. doi:10.1111/epi.13671

20. Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. *Epilepsia*. 2017;58(4):522-530. doi:10.1111/epi.13670

21. Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009. *Epilepsia*. 2010;51(4):676-685. doi:10.1111/j.1528-1167.2010.02522.x

22. Contreras Ramirez V, Vaddiparti A, Blumenfeld H. Testing awareness in focal seizures: Clinical practice and interpretation of current guidelines. *Ann Clin Transl Neurol*. 2022;9(5):762-765. doi:10.1002/acn3.51552

23. Beniczky S, Neufeld M, Diehl B, et al. Testing patients during seizures: A European consensus procedure developed by a joint taskforce of the ILAE – Commission on European Affairs and the European Epilepsy Monitoring Unit Association. *Epilepsia*. 2016;57(9):1363-1368. doi:10.1111/epi.13472

24. Mayville C, Fakhoury T, Abou-Khalil B. Absence seizures with evolution into generalized tonic-clonic activity: clinical and EEG features. *Epilepsia*. 2000;41(4):391-394. doi:10.1111/j.1528-1157.2000.tb00178.x

25. Steriade C, Sperling MR, DiVentura B, et al. Proposal for an updated seizure classification framework in clinical trials. *Epilepsia*. 2022;63(3):565-572. doi:10.1111/epi.17120

26. Beniczky S, Tatum WO, Blumenfeld H, et al. Seizure semiology: ILAE glossary of terms and their significance. *Epileptic Disord*. 2022;24(3):447-495. doi:10.1684/epd.2022.1430

27. Scheffer IE, Berkovic S, Capovilla G, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. *Epilepsia*. 2017;58(4):512-521. doi:10.1111/epi.13709

28. Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on

Classification and Terminology, 2005–2009. *Epilepsia*. 2010;51(4):676-685. doi:10.1111/j.1528-1167.2010.02522.x

29. Guerrini R, Dobyns WB. Malformations of cortical development: clinical features and genetic causes. *Lancet Neurol*. 2014;13(7):710-726. doi:10.1016/S1474-4422(14)70040-7

30. Grinton BE, Heron SE, Pelekanos JT, et al. Familial neonatal seizures in 36 families: Clinical and genetic features correlate with outcome. *Epilepsia*. 2015;56(7):1071-1080. doi:10.1111/epi.13020

31. Vezzani A, Fujinami RS, White HS, et al. Infections, inflammation and epilepsy. *Acta Neuropathol (Berl)*. 2016;131(2):211-234. doi:10.1007/s00401-015-1481-5

32. Lancaster E, Dalmau J. Neuronal autoantigens—pathogenesis, associated disorders and antibody testing. *Nat Rev Neurol*. 2012;8(7):380-390. doi:10.1038/nrneurol.2012.99

33. Kirschstein T, Köhling R. What is the Source of the EEG? *Clin EEG Neurosci*. 2009;40(3):146-149. doi:10.1177/155005940904000305

34. Pillai J, Sperling MR. Interictal EEG and the Diagnosis of Epilepsy. *Epilepsia*. 2006;47(s1):14-22. doi:10.1111/j.1528-1167.2006.00654.x

35. Hallez H, Vanrumste B, Grech R, et al. Review on solving the forward problem in EEG source analysis. *J NeuroEngineering Rehabil*. 2007;4(1):46. doi:10.1186/1743-0003-4-46

36. Harden CL, Huff JS, Schwartz TH, et al. Reassessment: Neuroimaging in the emergency patient presenting with seizure (an evidence-based review). *Neurology*. 2007;69(18):1772-1780. doi:10.1212/01.wnl.0000285083.25882.0e

37. Téllez-Zenteno JF, Ronquillo LH, Moien-Afshari F, Wiebe S. Surgical outcomes in lesional and non-lesional epilepsy: A systematic review and meta-analysis. *Epilepsy Res*. 2010;89(2):310-318. doi:10.1016/j.eplepsyres.2010.02.007

38. Bernasconi A, Cendes F, Theodore WH, et al. Recommendations for the use of structural magnetic resonance imaging in the care of patients with epilepsy: A consensus report from the International League Against Epilepsy Neuroimaging Task Force. *Epilepsia*. 2019;60(6):1054-1068. doi:10.1111/epi.15612

39. Blümcke I, Thom M, Aronica E, et al. International consensus classification of hippocampal sclerosis in temporal lobe epilepsy: A Task Force report from the ILAE Commission on Diagnostic Methods. *Epilepsia*. 2013;54(7):1315-1329. doi:10.1111/epi.12220

40. Thom M. Review: Hippocampal sclerosis in epilepsy: a neuropathology review. *Neuropathol Appl Neurobiol*. 2014;40(5):520-543. doi:10.1111/nan.12150

41. Kulaseharan S, Aminpour A, Ebrahimi M, Widjaja E. Identifying lesions in paediatric epilepsy using morphometric and textural analysis of magnetic resonance images. *NeuroImage Clin*. 2019;21:101663. doi:10.1016/j.nicl.2019.101663

42. Blumcke I, Spreafico R, Haaker G, et al. Histopathological Findings in Brain Tissue Obtained during Epilepsy Surgery. *N Engl J Med*. 2017;377(17):1648-1656. doi:10.1056/NEJMoa1703784

43. Contributors WE. Epilepsy Drugs to Treat Seizures. WebMD. Accessed December 24, 2024. https://www.webmd.com/epilepsy/medications-treat-seizures

44. https://fyra.io. Choosing Antiepileptic Drugs. Practical Neurology. Accessed December 24, 2024. https://practicalneurology.com/articles/2018-oct/choosing-antiepileptic-drugs

45. Krumholz A, Wiebe S, Gronseth GS, et al. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2015;84(16):1705-1713. doi:10.1212/WNL.0000000000001487

46. Larsson D, Mroué D, Andrén K, Zelano J. Antiseizure medication selection and retention for adult onset focal epilepsy in a Swedish health service region: A population-based cohort study. *Epilepsia*. 2023;64(10):2617-2624. doi:10.1111/epi.17711

47. Prevention. Accessed December 24, 2024. https://www.who.int/teams/mental-health-and-substance-use/treatment-care/mental-health-gap-action-programme/evidence-centre/epilepsy-and-seizures/antiseizure-medicines-for-management-of-epilepsy-in-adults-and-children

48. West S, Nevitt SJ, Cotton J, et al. Surgery for epilepsy. *Cochrane Database Syst Rev*. 2019;(6). doi:10.1002/14651858.cd010541.pub3

49. McIntosh AM, Wilson SJ, Berkovic SF. Seizure Outcome after Temporal Lobectomy: Current Research Practice and Findings. *Epilepsia*. 2001;42(10):1288-1307. doi:10.1046/j.1528-1157.2001.02001.x

50. Kwan P, Arzimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia*. 2010;51(6):1069-1077. doi:10.1111/j.1528-1167.2009.02397.x

51. Marson A, Jacoby A, Johnson A, Kim L, Gamble C, Chadwick D. Immediate versus deferred antiepileptic drug treatment for early epilepsy and single seizures: a randomised controlled trial. *The Lancet*. 2005;365(9476):2007-2013. doi:10.1016/S0140-6736(05)66694-9

52. McNamara P. *The Neuroscience of Sleep and Dreams*. Cambridge University Press; 2019. doi:10.1017/9781316817094

53. Metaphysical Supplement to the Theory of Dreams - ProQuest. Accessed December 25, 2024. https://www.proquest.com/openview/2e8f2fbb89e903a0664a3cf42455bd5d/1?pq-origsite=gscholar&cbl=1820903

54. Freud S. *The Interpretation of Dreams*.

55. Jouvet M. *Le Sommeil et le rêve*. O. Jacob; 1993.

56. Allan J. THE AMERICAN JOURNAL OF PSYCHIATRY.

57. Mbangmou RS, Wakeu MA, Ngeukeu R. Main Dream Theories and their Involvement in Psychological and Medical Clinics: A Need to Rethink the Function of Dreams? 2022;(4).

58. Godefroid J. *Psychologie: science humaine et science cognitive*. 3e éd. actualisée et augmentée. De Boeck; 2011.

59. Wamsley EJ. Dreaming and Offline Memory Consolidation. *Curr Neurol Neurosci Rep*. 2014;14(3):433. doi:10.1007/s11910-013-0433-5

60. Presleep Determinants of Dream Content: Effects of Two Films - David Foulkes, Allan Rechtschaffen, 1964. https://journals.sagepub.com/doi/abs/10.2466/pms.1964.19.3.983

61. Siclari F, Valli K, Arnulf I. Dreams and nightmares in healthy adults and in patients with sleep and neurological disorders. *Lancet Neurol*. 2020;19(10):849-859. doi:10.1016/S1474-4422(20)30275-1

62. Stickgold R, Malia A, Fosse R, Propper R, Hobson JA. Brain-Mind States: I. Longitudinal Field Study of Sleep/Wake Factors Influencing Mentation Report Length. *Sleep*. 2001;24(2):171-179. doi:10.1093/sleep/24.2.171

63. Siclari F, Baird B, Perogamvros L, et al. The neural correlates of dreaming. *Nat Neurosci*. 2017;20(6):872-878. doi:10.1038/nn.4545

64. Gaillard JM. Brain lateralization during sleep and dreaming. *Sleep*. 1989;88:177e81.

65. Doricchi: 8: Violani, C.(1992) Dream recall in brain—da... - Google Scholar. Accessed December 26, 2024. https://scholar.google.com/scholar_lookup?title=Dream%20recall%20in%20brain-damaged%20patients%3A%20a%20contribution%20to%20the%20neuropsychology%20of%20dreaming%20through%20a%20review%20of%20the%20literature&author=F.%20Doricchi&publication_year=1992&pages=99-129

66. Lavie P, Pratt H, Scharf B, Peled R, Brown J. Localized pontine 1esion. *Neurology*. 1984;34(1):118-118. doi:10.1212/WNL.34.1.118

67. Solms M. Dreaming and REM sleep are controlled by different brain mechanisms. *Behav Brain Sci*. 2000;23(6):843-850. doi:10.1017/S0140525X00003988

68. Bischof M, Bassetti CL. Total dream loss: A distinct neuropsychological dysfunction after bilateral PCA stroke. *Ann Neurol*. 2004;56(4):583-586. doi:10.1002/ana.20246

69. Leu-Semenescu S, Uguccioni G, Golmard JL, et al. Can we still dream when the mind is blank? Sleep and dream mentations in auto-activation deficit. *Brain*. 2013;136(10):3076-3084. doi:10.1093/brain/awt229

70. Greenberg MS, Farah MJ. The laterality of dreaming. *Brain Cogn*. 1986;5(3):307-321. doi:10.1016/0278-2626(86)90034-5

71. Murri L, Massetani R, Siciliano G, Giovanditti L, Arena R. Dream Recall After Sleep Interruption in Brain-Injured Patients. *Sleep*. 1985;8(4):356-362. doi:10.1093/sleep/8.4.356

72. Kosslyn SM, Ganis G, Thompson WL. Neural foundations of imagery. *Nat Rev Neurosci*. 2001;2(9):635-642. doi:10.1038/35090055

73. Kerr NH, Foulkes D. Right Hemispheric Mediation of Dream Visualization: A Case Study. *Cortex*. 1981;17(4):603-609. doi:10.1016/S0010-9452(81)80066-4

74. Solms M. Chapter 34 - Neurobiology and the neurological basis of dreaming. In: Montagna P, Chokroverty S, eds. *Handbook of Clinical Neurology*. Vol 98. Sleep Disorders Part I. Elsevier; 2011:519-544. doi:10.1016/B978-0-444-52006-7.00034-4

75. Solms M. *The Neuropsychology of Dreams: A Clinico-Anatomical Study*. Psychology Press; 2014. doi:10.4324/9781315806440

76. Murri L, Mancino M, Massetani R, Canapicchi R, et al. Effect of acute and chronic brain damage on dreaming. *Res Commun Psychol Psychiatry Behav*. 1989;14(2):121-142.

77. Cipolli C, Ferrara M, De Gennaro L, Plazzi G. Beyond the neuropsychology of dreaming: Insights into the neural basis of dreaming with new techniques of sleep recording and analysis. *Sleep Med Rev*. 2017;35:8-20. doi:10.1016/j.smrv.2016.07.005

78. Maquet P, Degueldre C, Delfiore G, et al. Functional Neuroanatomy of Human Slow Wave Sleep. *J Neurosci*. 1997;17(8):2807-2812. doi:10.1523/JNEUROSCI.17-08-02807.1997

79. Maquet P, Péters JM, Aerts J, et al. Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. *Nature*. 1996;383(6596):163-166. doi:10.1038/383163a0

80. Braun AR, Balkin TJ, Wesensten NJ, et al. Dissociated Pattern of Activity in Visual Cortices and Their Projections During Human Rapid Eye Movement Sleep. *Science*. 1998;279(5347):91-95. doi:10.1126/science.279.5347.91

81. Braun AR, Balkin TJ, Wesenten NJ, et al. Regional cerebral blood flow throughout the sleep-wake cycle. An H2(15)O PET study. *Brain*. 1997;120(7):1173-1197. doi:10.1093/brain/120.7.1173

82. Maquet P, Ruby P, Maudoux A, et al. Human cognition during REM sleep and the activity profile within frontal and parietal cortices: a reappraisal of functional neuroimaging data. In: Laureys S, ed. *Progress in Brain Research*. Vol 150. The Boundaries of Consciousness: Neurobiology and Neuropathology. Elsevier; 2005:219-595. doi:10.1016/S0079-6123(05)50016-5

83. Foulkes D, Vogel G. Mental activity at sleep onset. *J Abnorm Psychol*. 1965;70(4):231-243. doi:10.1037/h0022217

84. Pivik T, Foulkes D. NREM mentation: Relation to personality, orientation time, and time of night. *J Consult Clin Psychol*. 1968;32(2):144-151. doi:10.1037/h0025489

85. Antrobus J, Kondo T, Reinsel R, Fein G. Dreaming in the Late Morning: Summation of REM and Diurnal Cortical Activation. *Conscious Cogn*. 1995;4(3):275-299. doi:10.1006/ccog.1995.1039

86. Foulkes D, Fleisher S. Mental activity in relaxed wakefulness. *J Abnorm Psychol*. 1975;84(1):66-75. doi:10.1037/h0076164

87. Wu CW, Liu PY, Tsai PJ, et al. Variations in Connectivity in the Sensorimotor and Default-Mode Networks During the First Nocturnal Sleep Cycle. *Brain Connect*. 2012;2(4):177-190. doi:10.1089/brain.2012.0075

88. Koike T, Kan S, Misaki M, Miyauchi S. Connectivity pattern changes in default-mode network with deep non-REM and REM sleep. *Neurosci Res*. 2011;69(4):322-330. doi:10.1016/j.neures.2010.12.018

89. Picchioni D, Duyn JH, Horovitz SG. Sleep and the functional connectome. *NeuroImage*. 2013;80:387-396. doi:10.1016/j.neuroimage.2013.05.067

90. The neural substrate for dreaming: Is it a subsystem of the default network? - ScienceDirect. Accessed December 27, 2024. https://www.sciencedirect.com/science/article/pii/S1053810011000468?casa_token=LRV0bLLwOucAAAAA:x3lIXd6EvnZIVwWibZGLLczsgem89rpsSJEG3Ce3JtdHK2o-WISXeLoHZJuGgPhlqcmJKRPb

91. Koike T, Kan S, Misaki M, Miyauchi S. Connectivity pattern changes in default-mode network with deep non-REM and REM sleep. *Neurosci Res*. 2011;69(4):322-330. doi:10.1016/j.neures.2010.12.018

92. Pace-Schott EF. The Neurobiology of Dreaming. In: *Principles and Practice of Sleep Medicine*. Elsevier; 2011:563-575. doi:10.1016/B978-1-4160-6645-3.00048-7

93. Hobson JA, Pace-Schott EF, Stickgold R. Dreaming and the brain: Toward a cognitive neuroscience of conscious states. *Behav Brain Sci*. 2000;23(6):793-842. doi:10.1017/S0140525X00003976

94. Schwartz S, Maquet P. Sleep imaging and the neuro-psychological assessment of dreams. *Trends Cogn Sci*. 2002;6(1):23-30. doi:10.1016/S1364-6613(00)01818-0

95. Pace-Schott EF. The frontal lobes and dreaming. In: *The New Science of Dreaming: Volume 1. Biological Aspects*. Praeger perspectives. Praeger Publishers/Greenwood Publishing Group; 2007:115-154.

96. Eichenlaub JB, Bertrand O, Morlet D, Ruby P. Brain Reactivity Differentiates Subjects with High and Low Dream Recall Frequencies during Both Sleep and Wakefulness. *Cereb Cortex*. 2014;24(5):1206-1215. doi:10.1093/cercor/bhs388

97. Eichenlaub JB, Nicolas A, Daltrozzo J, Redouté J, Costes N, Ruby P. Resting Brain Activity Varies with Dream Recall Frequency Between Subjects. *Neuropsychopharmacology*. 2014;39(7):1594-1602. doi:10.1038/npp.2014.6

98. Dopaminergic system and dream recall: An MRI study in Parkinson's disease patients. doi:10.1002/hbm.23095

99. De Gennaro L, Cipolli C, Cherubini A, et al. Amygdala and hippocampus volumetry and diffusivity in relation to dreaming. *Hum Brain Mapp*. 2011;32(9):1458-1470. doi:10.1002/hbm.21120

100. Sateia MJ. International Classification of Sleep Disorders-Third Edition. *Chest*. 2014;146(5):1387-1394. doi:10.1378/chest.14-0970

101. Can observers link dream content to behaviours in rapid eye movement sleep behaviour disorder? A cross-sectional experimental pilot study - VALLI - 2012 - Journal of Sleep Research - Wiley Online Library. Accessed December 28, 2024. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2869.2011.00938.x?casa_token=B7r--2jo-uAAAAAA%3A6EFz8v6dvyhPP-WYXoqNZhzkoSpAmXIplfttbUf5B8V-WZN8ljyvOgI6UjiOAqFcL0GrxWD5ZFMoZw

102. Postuma RB, Iranzo A, Hu M, et al. Risk and predictors of dementia and parkinsonism in idiopathic REM sleep behaviour disorder: a multicentre study. *Brain*. 2019;142(3):744-759. doi:10.1093/brain/awz030

103. Ehrminger M, Latimier A, Pyatigorskaya N, et al. The coeruleus/subcoeruleus complex in idiopathic rapid eye movement sleep behaviour disorder. *Brain*. 2016;139(4):1180-1188. doi:10.1093/brain/aww006

104. Postuma RB, Arnulf I, Hogl B, et al. A single-question screen for rapid eye movement sleep behavior disorder: A multicenter validation study. *Mov Disord*. 2012;27(7):913-916. doi:10.1002/mds.25037

105. Schenck CH, Mahowald MW. REM Sleep Behavior Disorder: Clinical, Developmental, and Neuroscience Perspectives 16 Years After its Formal Identification in SLEEP. *Sleep*. 2002;25(2):120-138. doi:10.1093/sleep/25.2.120

106. Oudiette D, De Cock VC, Lavault S, Leu S, Vidailhet M, Arnulf I. Nonviolent elaborate behaviors may also occur in REM sleep behavior disorder. *Neurology*. 2009;72(6):551-557. doi:10.1212/01.wnl.0000341936.78678.3a

107. Uguccioni G, Golmard JL, De Fontréaux AN, Leu-Semenescu S, Brion A, Arnulf I. Fight or flight? Dream content during sleepwalking/sleep terrors vs rapid eye movement sleep behavior disorder. *Sleep Med*. 2013;14(5):391-398. doi:10.1016/j.sleep.2013.01.014

108. Sharf B, Moskovitz Ch, Lupton MD, Klawans HL. Dream phenomena induced by chronic levodopa therapy. *J Neural Transm*. 1978;43(2):143-151. doi:10.1007/BF01579073

109. Dopaminergic system and dream recall: An MRI study in Parkinson's disease patients. doi:10.1002/hbm.23095

110. De Cock VC, Vidailhet M, Leu S, et al. Restoration of normal motor control in Parkinson's disease during REM sleep. *Brain*. 2007;130(2):450-456. doi:10.1093/brain/awl363

111. Forsaa EB, Larsen JP, Wentzel-Larsen T, et al. A 12-Year Population-Based Study of Psychosis in Parkinson Disease. *Arch Neurol*. 2010;67(8):996-1001. doi:10.1001/archneurol.2010.166

112. Anang JBM, Gagnon JF, Bertrand JA, et al. Predictors of dementia in Parkinson disease. *Neurology*. 2014;83(14):1253-1260. doi:10.1212/WNL.0000000000000842

113. Zadra A, Desautels A, Petit D, Montplaisir J. Somnambulism: clinical aspects and pathophysiological hypotheses. *Lancet Neurol*. 2013;12(3):285-294. doi:10.1016/S1474-4422(12)70322-8

114. Oudiette D, Leu S, Pottier M, Buzare MA, Brion A, Arnulf I. Dreamlike Mentations During Sleepwalking and Sleep Terrors in Adults. *Sleep*. 2009;32(12):1621-1627. doi:10.1093/sleep/32.12.1621

115. Parrino L, Terzano MG. *The international classification of sleep disorders*. WESTCHESTER (IL); 2005. Accessed December 28, 2024. https://air.unipr.it/handle/11381/2293024

116. Dodet P, Chavez M, Leu-Semenescu S, Golmard JL, Arnulf I. Lucid Dreaming in Narcolepsy. *Sleep*. 2015;38(3):487-497. doi:10.5665/sleep.4516

117. Rak M, Beitinger P, Steiger A, Schredl M, Dresler M. Increased Lucid Dreaming Frequency in Narcolepsy. *Sleep*. 2015;38(5):787-792. doi:10.5665/sleep.4676

118. Cipolli C, Bellucci C, Mattarozzi K, Mazzetti M, Tuozzi G, Plazzi G. Story-like organization of REM-dreams in patients with narcolepsy–cataplexy. *Brain Res Bull*. 2008;77(4):206-213. doi:10.1016/j.brainresbull.2008.07.012

119. Fosse R, Stickgold R, Hobson JA. Emotional Experience During Rapid-eye-movement Sleep in Narcolepsy. *Sleep*. 2002;25(7):724-732. doi:10.1093/sleep/25.7.724

120. Wamsley E, Donjacour CEHM, Scammell TE, Lammers GJ, Stickgold R. Delusional Confusion of Dreaming and Reality in Narcolepsy. *Sleep*. 2014;37(2):419-422. doi:10.5665/sleep.3428

121. Stumbrys T, Erlacher D, Schädlich M, Schredl M. Induction of lucid dreams: A systematic review of evidence. *Conscious Cogn*. 2012;21(3):1456-1475. doi:10.1016/j.concog.2012.07.003

122. Lacaux C, Izabelle C, Santantonio G, et al. Increased creative thinking in narcolepsy. *Brain*. 2019;142(7):1988-1999. doi:10.1093/brain/awz137

123. Bazil CW, Castro LHM, Walczak TS. Reduction of Rapid Eye Movement Sleep by Diurnal and Nocturnal Seizures in Temporal Lobe Epilepsy. *Arch Neurol*. 2000;57(3):363-368. doi:10.1001/archneur.57.3.363

124. Tian N, Wheaton AG, Zack M, Croft JB, Greenlund KJ. Sleep duration and quality among U.S. adults with epilepsy: National Health Interview Survey 2013, 2015, and 2017. *Epilepsy Behav*. 2021;122:108194. doi:10.1016/j.yebeh.2021.108194

125. Bazil CW. Epilepsy and sleep disturbance. *Epilepsy Behav*. 2003;4:39-45. doi:10.1016/j.yebeh.2003.07.005

126. Shvarts V, Chung S. Epilepsy, Antiseizure Therapy, and Sleep Cycle Parameters. *Epilepsy Res Treat*. 2013;2013(1):670682. doi:10.1155/2013/670682

127. Manni R, Terzaghi M. Comorbidity between epilepsy and sleep disorders. *Epilepsy Res*. 2010;90(3):171-177. doi:10.1016/j.eplepsyres.2010.05.006

128. de la Chapelle A, Frauscher B, Valomon A, Ruby PM, Peter-Derex L. Relationship Between Epilepsy and Dreaming: Current Knowledge, Hypotheses, and Perspectives. *Front Neurosci*. 2021;15. doi:10.3389/fnins.2021.717078

129. Nir Y, Tononi G. Dreaming and the brain: from phenomenology to neurophysiology. *Trends Cogn Sci*. 2010;14(2):88-100. doi:10.1016/j.tics.2009.12.001

130. Solms M. Dreaming and REM sleep are controlled by different brain mechanisms. *Behav Brain Sci*. 2000;23(6):843-850. doi:10.1017/S0140525X00003988

131. Bentes C, Costa J, Peralta R, Pires J, Sousa P, Paiva T. Dream recall frequency and content in patients with temporal lobe epilepsy: Dreams and Temporal Lobe Epilepsy. *Epilepsia*. 2011;52(11):2022-2027. doi:10.1111/j.1528-1167.2011.03290.x

132. Cipolli C, Bonanni E, Maestri M, Mazzetti M, Murri L. Dream experience during REM and NREM sleep of patients with complex partial seizures. *Brain Res Bull*. 2004;63(5):407-413. doi:10.1016/j.brainresbull.2003.12.014

133. EPSTEIN AW, HILL W. Ictal Phenomena During REM Sleep of a Temporal Lobe Epileptic. *Arch Neurol*. 1966;15(4):367-375. doi:10.1001/archneur.1966.00470160033005

134. Vercueil L. Dreaming of seizures. *Epilepsy Behav*. 2005;7(1):127-128. doi:10.1016/j.yebeh.2005.04.003

135. Nielsen TA. THE NEUROPSYCHOLOGY OF DREAMS. 1997. By: Mark Solms. Published by Lawrence Erlbaum Associates. 292 pages. $C78.00. *Can J Neurol Sci J Can Sci Neurol*. 1998;25(4):346-347. doi:10.1017/S0317167100034454

136. Curot J, Valton L, Denuelle M, et al. Déjà-rêvé: Prior dreams induced by direct electrical brain stimulation. *Brain Stimul Basic Transl Clin Res Neuromodulation*. 2018;11(4):875-885. doi:10.1016/j.brs.2018.02.016

137. Paiva T, Bugalho P, Bentes C. Dreaming and cognition in patients with frontotemporal dysfunction. *Conscious Cogn*. 2011;20(4):1027-1035. doi:10.1016/j.concog.2011.06.008

138. Bonanni E, Cipolli C, Iudice A, Mazzetti M, Murri L. Dream Recall Frequency in Epilepsy Patients with Partial and Generalized Seizures: A Dream Diary Study. *Epilepsia*. 2002;43(8):889-895. doi:10.1046/j.1528-1157.2002.48101.x

139. Elce V, Bergamo D, Bontempi G, et al. The individual determinants of morning dream recall. *Commun Psychol*. 2025;3(1):25. doi:10.1038/s44271-025-00191-z

140. Bernasconi A, Cendes F, Theodore WH, et al. Recommendations for the use of structural magnetic resonance imaging in the care of patients with epilepsy: A consensus report from the International League Against Epilepsy Neuroimaging Task Force. *Epilepsia*. 2019;60(6):1054-1068. doi:10.1111/epi.15612

141. Lancu I, Olmer A. [The minimental state examination--an up-to-date review]. *Harefuah*. 2006;145(9):687-690, 701.

142. Molloy DW, Standish TIM. A Guide to the Standardized Mini-Mental State Examination. *Int Psychogeriatr*. 1997;9(S1):87-94. doi:10.1017/S1041610297004754

143. Kurlowicz L, Wallace M. The Mini Mental State Examination (MMSE).

144. Sala SD, Laiacona M, Spinnler H, Ubezio C. A cancellation test: its reliability in assessing attentional deficits in Alzheimer's disease. *Psychol Med*. 1992;22(4):885-901. doi:10.1017/S0033291700038460

145. Jensen AR. SCORING THE STROOP TEST.

146. Scarpina F, Tagini S. The Stroop Color and Word Test. *Front Psychol*. 2017;8:557. doi:10.3389/fpsyg.2017.00557

147. Ghimire N, Paudel BH, Khadka R, Singh PN. Reaction time in Stroop test in Nepalese Medical Students. *J Clin Diagn Res JCDR*. 2014;8(9):BC14-BC16. doi:10.7860/JCDR/2014/10615.4891

148. Caffarra P, Vezzadini G, Dieci F, Zonato F, Venneri A. A short version of the Stroop test: Normative data in an Italian population sample. Published online 2002. Accessed June 5, 2025. https://air.unipr.it/handle/11381/2989715

149. Novelli G, Papagno C, Capitani E, Laiacona M, et al. Tre test clinici di memoria verbale a lungo termine: Taratura su soggetti normali. [Three clinical tests for the assessment of verbal long-term memory function: Norms from 320 normal subjects.]. *Arch Psicol Neurol Psichiatr*. 1986;47(2):278-296.

150. Del Signore F, Rosi A, Palumbo R, et al. Capacity to consent to research in older adults with normal cognitive functioning, mild and major neurocognitive disorder: an Italian study. *Mediterr J Clin Psychol*. 2023;Vol 11:No 1 (2023). doi:10.13129/2282-1619/MJCP-3620

151. de Renzi E, Faglioni P, Ruggerini C. Studies of verbal memory in clinical application for the diagnosis of amnesia. *Arch Psicol Neurol Psichiatr*. 1977;38(3):303-318.

152. Somerville J. *A Comparison of Administration Procedures for the Rey-Osterrieth Complex Figure: Flow-Charts vs. Pen-Switching*. University of Rhode Island; 2000. doi:10.23860/thesis-somerville-jessica-2000

153. Opîrlesc AD. Automating the Evaluation of Rey- Osterrieth Complex Figure Test Using a Decision Support System for Portable Devices.

154. Bertolani L, de Renzi E, Faglioni P. Test di memoria non verbale di impiego diagnostico in clinica: taratura su soggetti normali. [Normative data on nonverbal memory tests of clinical interest.]. *Arch Psicol Neurol Psichiatr*. 1993;54(4):477-486.

155. Costa A, Bagoj E, Monaco M, et al. Standardization and normative data obtained in the Italian population for a new verbal fluency instrument, the phonemic/semantic alternate fluency test. *Neurol Sci*. 2014;35(3):365-372. doi:10.1007/s10072-013-1520-8

156. Jackson-Koku G. Beck Depression Inventory. *Occup Med*. 2016;66(2):174-175. doi:10.1093/occmed/kqv087

157. Beck Depression Inventory - an overview | ScienceDirect Topics. Accessed May 22, 2025. https://www.sciencedirect.com/topics/psychology/beck-depression-inventory

158. Spielberger CD. State-Trait Anxiety Inventory for Adults. Published online July 9, 2012. doi:10.1037/t06496-000

159. Kayikcioglu O, Bilgin S, Seymenoglu G, Deveci A. State and Trait Anxiety Scores of Patients Receiving Intravitreal Injections. *Biomed Hub*. 2017;2(2):1-5. doi:10.1159/000478993

160. Spielberger CD, Gonzalez-Reigosa F, Martinez-Urrutia A, Natalicio LFS, Natalicio DS. The State-Trait Anxiety Inventory. *Rev Interam Psicol J Psychol*. 2017;5(3 & 4). doi:10.30849/rip/ijp.v5i3

161. JULIAN LJ. Measures of Anxiety. *Arthritis Care Res*. 2011;63(0 11):10.1002/acr.20561. doi:10.1002/acr.20561

162. Bulkeley K, Schredl M. Attitudes towards dreaming: Effects of socio-demographic and religious variables in an American sample. *Int J Dream Res*. Published online April 30, 2019:75-81. doi:10.11588/ijodr.2019.1.54314

163. Schredl M. Positive and negative attitudes towards dreaming: A representative study. *Dreaming*. 2013;23(3):194-201. doi:10.1037/a0032477

164. Governale J. *Students' Orientations toward Dreams and the Development of Scales for Their Measurement*.; 2000. doi:10.15760/etd.5981

165. schredl2002.

166. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*. 1991;14(6):540-545. doi:10.1093/sleep/14.6.540

167. About the ESS – Epworth Sleepiness Scale. Accessed May 24, 2025. https://epworthsleepinessscale.com/about-the-ess/

168. Carriere JSA, Seli P, Smilek D. Wandering in both mind and body: Individual differences in mind wandering and inattention predict fidgeting. *Can J Exp Psychol Rev Can Psychol Expérimentale*. 2013;67(1):19-31. doi:10.1037/a0031438

169. Seli P, Carriere JSA, Smilek D. Not all mind wandering is created equal: dissociating deliberate from spontaneous mind wandering. *Psychol Res*. 2015;79(5):750-758. doi:10.1007/s00426-014-0617-x

170. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28(2):193-213. doi:10.1016/0165-1781(89)90047-4

171. Marks DF. Vividness of Visual Imagery Questionnaire. Published online March 10, 2014. doi:10.1037/t05959-000

172. Marks DF. VISUAL IMAGERY DIFFERENCES IN THE RECALL OF PICTURES. *Br J Psychol*. 1973;64(1):17-24. doi:10.1111/j.2044-8295.1973.tb01322.x

173. Horne JA, Ostberg O. A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *Int J Chronobiol*. 1976;4(2):97-110.

174. Shahid A, Wilkinson K, Marcu S, Shapiro CM. Morningness-Eveningness Questionnaire. In: Shahid A, Wilkinson K, Marcu S, Shapiro CM, eds. *STOP, THAT and One Hundred Other Sleep Scales*. Springer New York; 2011:231-234. doi:10.1007/978-1-4419-9893-4_54

175. IBM SPSS Statistics. April 5, 2024. Accessed May 25, 2025. https://www.ibm.com/products/spss-statistics

176. Fischl B. FreeSurfer. *NeuroImage*. 2012;62(2):774-781. doi:10.1016/j.neuroimage.2012.01.021

177. Desikan RS, Ségonne F, Fischl B, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage*. 2006;31(3):968-980. doi:10.1016/j.neuroimage.2006.01.021

178. Iglesias JE, Augustinack JC, Nguyen K, et al. A computational atlas of the hippocampal formation using ex vivo , ultra-high resolution MRI: Application to adaptive segmentation of in vivo MRI. *NeuroImage*. 2015;115:117-137. doi:10.1016/j.neuroimage.2015.04.042

179. Saygin ZM, Kliemann D, Iglesias JE, et al. High-resolution magnetic resonance imaging reveals nuclei of the human amygdala: manual segmentation to automatic atlas. *NeuroImage*. 2017;155:370-382. doi:10.1016/j.neuroimage.2017.04.046

180. Micalizzi E, Ballerini A, Giovannini G, et al. The role of the amygdala in ictal central apnea: insights from brain MRI morphometry. *Ann Clin Transl Neurol*. 2023;11(1):121-132. doi:10.1002/acn3.51938

181. Ballerini A, Biagioli N, Carbone C, et al. Late-onset temporal lobe epilepsy: insights from brain atrophy and Alzheimer's disease biomarkers. *Brain*. 2025;148(1):185-198. doi:10.1093/brain/awae207

182. Ballerini A, Tondelli M, Talami F, et al. Amygdala subnuclear volumes in temporal lobe epilepsy with hippocampal sclerosis and in non-lesional patients. *Brain Commun*. 2022;4(5):fcac225. doi:10.1093/braincomms/fcac225

183. Ballerini A, Talami F, Molinari MA, et al. Exploring the relationship between amygdala subnuclei volumes and cognitive performance in left-lateralized temporal lobe epilepsy with and without hippocampal sclerosis. *Epilepsy Behav*. 2023;145:109342. doi:10.1016/j.yebeh.2023.109342

184. Micalizzi E, Ballerini A, Giovannini G, et al. The role of the amygdala in ictal central apnea: insights from brain MRI morphometry. *Ann Clin Transl Neurol*. 2024;11(1):121-132. doi:10.1002/acn3.51938

185. Price JL, Russchen FT, Amaral DG. *The Limbic Region. II: The Amygdaloid Complex.* Elsevier Sci.; 1987.

186. Benarroch EE. The amygdala: Functional organization and involvement in neurologic disorders. *Neurology*. 2015;84(3):313-324. doi:10.1212/WNL.0000000000001171

187. Motamedi G, Meador K. Epilepsy and cognition. *Epilepsy Behav*. 2003;4:25-38. doi:10.1016/j.yebeh.2003.07.004

188. Salpekar JA, Basu T, Thangaraj S, Maguire J. Chapter Eight - The intersections of stress, anxiety and epilepsy. In: Clow A, Smyth N, eds. *International Review of Neurobiology*. Vol 152. Stress and Brain Health: In Clinical Conditions. Academic Press; 2020:195-219. doi:10.1016/bs.irn.2020.02.001

189. Ciuffini R, Stratta P, Marrelli A. Emotional reactivity in mesial temporal lobe epilepsy: A pilot study. *Epilepsy Behav EB*. 2018;82:87-90. doi:10.1016/j.yebeh.2018.02.011

190. de la Chapelle A, Frauscher B, Valomon A, Ruby PM, Peter-Derex L. Relationship Between Epilepsy and Dreaming: Current Knowledge, Hypotheses, and Perspectives. *Front Neurosci*. 2021;15:717078. doi:10.3389/fnins.2021.717078

191. Solms M. Chapter 34 - Neurobiology and the neurological basis of dreaming. In: Montagna P, Chokroverty S, eds. *Handbook of Clinical Neurology*. Vol 98. Sleep Disorders Part I. Elsevier; 2011:519-544. doi:10.1016/B978-0-444-52006-7.00034-4

192. Christoff K, Irving ZC, Fox KCR, Spreng RN, Andrews-Hanna JR. Mind-wandering as spontaneous thought: a dynamic framework. *Nat Rev Neurosci*. 2016;17(11):718-731. doi:10.1038/nrn.2016.113

193. Christoff K. Thinking. In: *The Oxford Handbook of Cognitive Neuroscience, Vol. 2: The Cutting Edges*. Oxford library of psychology. Oxford University Press; 2014:318-333.

194. Meisner OC, Nair A, Chang SWC. Amygdala connectivity and implications for social cognition and disorders. *Handb Clin Neurol*. 2022;187:381-403. doi:10.1016/B978-0-12-823493-8.00017-1

195. Etkin A, Klemenhagen KC, Dudman JT, et al. Individual Differences in Trait Anxiety Predict the Response of the Basolateral Amygdala to Unconsciously Processed Fearful Faces. *Neuron*. 2004;44(6):1043-1055. doi:10.1016/j.neuron.2004.12.006

196. Ntwatwa Z, Spreckelmeyer JM, Bas-Hoogendam JM, et al. Specific amygdala and hippocampal subfield volumes in social anxiety disorder and their relation to clinical characteristics – an international mega-analysis. Published online February 2, 2024:2024.01.29.576056. doi:10.1101/2024.01.29.576056

197. Hu Y, Moore M, Bertels Z, Phan KL, Dolcos F, Dolcos S. Smaller amygdala volume and increased neuroticism predict anxiety symptoms in healthy subjects: A volumetric approach using manual tracing. *Neuropsychologia*. 2020;145:106564. doi:10.1016/j.neuropsychologia.2017.11.008

198. Yang RJ, Mozhui K, Karlsson RM, Cameron HA, Williams RW, Holmes A. Variation in mouse basolateral amygdala volume is associated with differences in stress reactivity and fear learning. *Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol*. 2008;33(11):2595-2604. doi:10.1038/sj.npp.1301665

199. Herlin B, Navarro V, Dupont S. The temporal pole: From anatomy to function-A literature appraisal. *J Chem Neuroanat*. 2021;113:101925. doi:10.1016/j.jchemneu.2021.101925

200. Dolcos F, LaBar KS, Cabeza R. Interaction between the amygdala and the medial temporal lobe memory system predicts better memory for emotional events. *Neuron*. 2004;42(5):855-863. doi:10.1016/s0896-6273(04)00289-2

201. Aminoff EM, Kveraga K, Bar M. The role of the parahippocampal cortex in cognition. *Trends Cogn Sci*. 2013;17(8):379-390. doi:10.1016/j.tics.2013.06.009

202. den Stock JV, Vandenbulcke M, Sinke CBA, de Gelder B. Affective scenes influence fear perception of individual body expressions. *Hum Brain Mapp*. 2012;35(2):492-502. doi:10.1002/hbm.22195

203. Andrews-Hanna JR, Reidler JS, Sepulcre J, Poulin R, Buckner RL. Functional-Anatomic Fractionation of the Brain's Default Network. *Neuron*. 2010;65(4):550-562. doi:10.1016/j.neuron.2010.02.005

204. Buckner RL, Andrews-Hanna JR, Schacter DL. The Brain's Default Network. *Ann N Y Acad Sci*. 2008;1124(1):1-38. doi:10.1196/annals.1440.011

205. Šimić G, Tkalčić M, Vukić V, et al. Understanding Emotions: Origins and Roles of the Amygdala. *Biomolecules*. 2021;11(6):823. doi:10.3390/biom11060823

206. Fox KCR, Andrews-Hanna JR, Mills C, et al. Affective neuroscience of self-generated thought. *Ann N Y Acad Sci*. Published online May 12, 2018. doi:10.1111/nyas.13740