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Clinical and Neuropsychological Assessment in Epilepsy

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Abstract

A large number of publications have dealt with cognition in epilepsy. Most factors affecting cognition in epilepsy have been discerned many years ago. The body of neuropsychological literature in this field has accumulated much knowledge, in the epilepsy surgery settings, neuropsychology has still not been fully integrated in the routine care of patients with epilepsy. The comorbidities of epilepsy are becoming an increasingly relevant topic. Epilepsy may be defined by the occurrence of epileptic seizures, these seizures represent only one of several possible sources of cognitive impairment. There are complex interactions between epilepsy, cognition and behavior, and that both seizures and problems with cognition or behavior may result from a common underlying pathology requiring treatment.

The objective of this review is to summarize clinically relevant diagnostic and we aim to demonstrate that neuropsychology can make a highly valuable contribution to the care of individual patients by contributing to the diagnostic process and by serving as a tool for the monitoring of disease and treatment, thereby improving the quality and safety of patient care and their caregiver.

Keywords: *Epilepsy, Cognition, Neuropsycological Assessment.*

Introduction

Epilepsy and Epileptic seizures: definitions Epilepsy is derived from the Greek verb ἐπιλαμβάνειν (epi- lambanein) meaning "to be taken by surprise," "to be struck by something," "to be overwhelmed" (1), these aspects highlight the characteristic of the pathology, which manifests itself in the absence of anticipatory signs, resulting in the subject being overwhelmed, the tendency to recur and spontaneously ceasing. Definitions of epilepsy are variable and subject to change.

Michael Trimble, in an article published in Epilepsia, described the cognitive hazards of seizure disorders, identifying the major factors to be considered with cognitive impairment in epilepsy in two groups of patients with this disorder, i.e. underlying brain damage, age at seizure onset, seizure type and frequency, as well as antiepileptic drugs (AEDs) (2).

This study already revealed an understanding of the complex and multifactorial etiology of cognitive impairment and decline in epilepsy.

The question of decline in epilepsy is old and was discussed as "epileptic dementia" in medical texts as early as at the turn of the 19th century. At that time epileptic dementia was thought to manifest in 50% of all patients (3,4).

Clinical practice is not sufficient to treat seizures to resolve the cognitive problems seen in patients with epilepsy, neuropsychology represents an independent approach to the patient, his disorder and its underlying pathology and may call for therapeutic interventions other than those primarily directed at reducing the number of seizures.

SEMEIOLOGY OF EPILEPTIC SEIZURES

Seizures are defined by the ILAE as the transient occurrence of signs/symptoms due to abnormal, excessive, or hypersynchronous electrical activity in the brain.

According to the most recent classification, the main distinction is according to the brain area involved by the epileptogenic focus, i.e., the aggregate of neurons from which the discharge originates; thus, one can have seizures with focal, generalized, or unknown onset.

These in turn are divided into motor or nonmotor seizures, which can lead to different manifestations (5,6).

Although in the common imagination epilepsy is often associated with seizures, typical of generalized tonic-clonic seizures (also called "big bad"), this can announce itself with quite different symptoms such as behavioral arrest, automatisms, dejavu, sensory hallucinations, and sudden changes in mood, typical of focal seizures; or as loss of contact with the outside world and motor arrest, typical of generalized absence seizures.

Epidemiological data show that the incidence of focal rather than generalized seizures is higher (7).

One reason epilepsy education is difficult is the complexity and nuanced knowledge required to recognize and deal with different forms of seizures.

At the same time, however, the diagnosis of an epilepsy and the location of the epileptogenic focus relies heavily on the witness's description of the event.

Obtaining an appropriate account of the events from a witness is a crucial component of patient assessment, particularly because most seizures do not last long enough to be identified by first responders and patients are unable to provide useful information because they present to the emergency in a post-ictal and confused state with no memory of the event.

Although assessment tools such as EEG or brain imaging can help, they are not always diagnostic (8).

Although it is important to investigate seizure risk factors or look for clinical signs that suggest a seizure has occurred, knowing the semiological details can direct identification of the most appropriate treatment.

A seizure in the real world is a very dramatic event for a first-time witness, and the emotional impact can affect the details of observation. In addition, witnesses often do not spontaneously provide all the necessary information without being asked (8,9,10,11,12).

The new classification, therefore, recognizes that there is not only the generalized convulsive type epileptic state, although it is the most damaging, but also typically nonconvulsive forms. In this regard, the importance of EEG recordings is emphasized because although they are difficult to obtain for some forms of status epilepticus such as convulsive, for others they are the only means of diagnosing them.

Therefore, obtaining them as early as possible is crucial in approaching the patient, as they influence the choice and aggressiveness of treatment, prognosis, and clinical approaches.

The general population should first be informed about the various types of seizures and their symptoms; then they should receive appropriate first-aid training for all the different forms. Finally, they should be instructed to observe behaviors preceding and accompanying seizure episodes in order to be able to report information useful for diagnosis and/or lateralization of the phenomenon. To carry out these educational interventions, instead of the usual information dossiers, social media could be exploited to share lessons in the form of posts or short videos; or a significantly larger section of the population would be sensitized by airing educational films between television programs. Another idea might be to create a free online course that would allow interactive learning of the concepts, through quizzes or branching scenarios. Then, to ensure practical application of the rescue maneuvers, it would be useful to include in the BLSD and PBLSD courses already popular in schools and workplaces the part on epileptic seizure management.

Pathophysiology of epileptic discharge

Epileptic seizure is caused by a condition of neuronal hyperexcitability, defined as the tendency of a neuronal aggregate to discharge repeatedly and hyper synchronously in response to a stimulus that should generate a single action potential (13).

Epilepsy and its manifestations are an expression of an alteration of the normal balance between excitatory and inhibitory processes, which regulate brain functions (14).

Spread of epileptic access

If the abnormal, synchronized electrical activity remains confined to the neuronal aggregate, which forms the focus of the epileptic access, no clinical manifestations are evident.

Classification of epileptic accesses and epilepsies.

The International League Against Epilepsy (ILAE) has proposed an operational classification of epileptic seizures and epilepsies, based on studies from 1981 to 2017 followed by careful revisions (6).

The goal was to develop a tool applicable to the clinical setting that provides understandable explanations, defines seizure types, triggers and risk of comorbidities). Comorbidities include learning disabilities, intellectual disability, neuropsychiatric symptoms such as autism spectrum disorders, and mortality risk such as sudden death in epilepsy). The first attempt at Noso graphic classification, in 1970, was by Gastaut who distinguished epilepsy from seizure by etiology and location of the lesion (15). Recent studies, have shown that epilepsy is not the symptom of local brain abnormalities, but a network disease with a possible neocortical, thalamocortical, limbic, and brainstem origin (6).

Etiology of epilepsy

The International League Against Epilepsy (ILAE) (16) in its 2017 review, identified six distinct etiological groups based on potential therapeutic implications, distinguishing between:

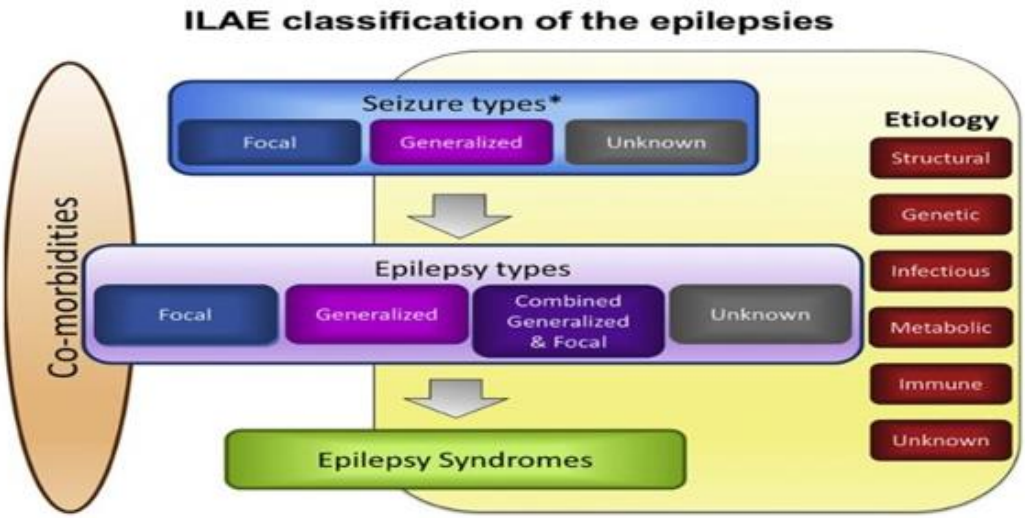

Figure 1: Classification of epilepsies organized into levels: seizure types, epilepsy types, and epilepsy syndromes (6)

For diagnostic purposes, the first level identifies seizure type, distinguished in relation to onset characteristics; in it, seizures are divided into:
1) focal onset seizures;
2) generalized onset seizures;
3) Crises with unknown onset;

The classification is based on the results to electroencephalographic (EEG) investigations and from neuroimaging studies, the clinician makes a diagnosis of the type of epilepsy distinguished into:
1) focal epilepsy;
2) generalized epilepsy;
3) combined epilepsy (focal and generalized);
4) epilepsy of unknown type;

Finally, in the third level, a specific syndromic diagnosis can be made. In each level, the etiology is associated, divided into six subgroups:
1) Structural;
2) Genetic;
3) Infectious;
4) Metabolic;
5) Autoimmune;
6) Unknown;

Structural etiology
Experimental Studies have shown that the presence of a structural abnormality carries an increased risk of developing epilepsy. This can be caused by vascular lesions (stroke or anoxo-ischemic encephalopathy), traumatic or infectious meningitis), genetic such as malformations of cortical development, and neurocutaneous syndromes (neurofibromatosis, tuberous sclerosis, or Sturge- Weber syndrome).

For example, epilepsies with structural etiology include hippocampal sclerosis associated with mesial temporal lobe seizures, which is one of the most frequent causes of drug-resistant focal epilepsy. Prenatal factors include disturbances in embryonic or fetal development with structural malformations of the cerebral cortex or vascular system; perinatal factors include perinatal ataxia, hypoxic-ischemic-hemorrhagic syndrome, and cerebral edema; and postnatal risk factors include cerebral head trauma, meningo-encephalitis, cerebral tumors, and metabolic or toxic disorders. In adolescence, non-developmental structural lesions, acquired in the first months of life, are observed. Finally, in later life the most frequent causes are tumors, neurodegenerative diseases, and cerebrovascular diseases.

Genetic etiology
Genetic epilepsies, originally termed idiopathic, are genetically determined, can be generalized and focal, age-dependent, and not associated with neurological diseases

Infectious etiology
Infectious etiology is directly related to an infection of the central nervous system. It can be caused by diseases such as neurocysticercosis, tuberculosis, cerebral toxoplasmosis, and congenital infections such as Zika virus and cytomegalovirus.

Metabolic etiology
In metabolic etiology, seizures are the consequence of a known or presumed metabolic disorder, caused, for example, by porphyria, uremia, aminoacidopathies, or pyridoxine-dependent seizures. In many cases, metabolic disorders have a genetic cause.

Immune etiology: The category includes immune-mediated conditions in which seizures are caused by an immune disorder, the most representative examples include encephalitis with anti-LGI1 antibodies and with anti-NMDA antibodies.

Unknown etiology: epilepsies, traditionally termed cryptogenic, have unknown causes that cannot be demonstrated by instrumental investigations. They include focal epilepsies, with unknown etiology, with features not corresponding to idiopathic partial epilepsy

First level of classification: identification of seizure type

Focal onset seizures: In 2010 The International League Against Epilepsy defined the term "focal" as "originating within networks limited to one hemisphere" (6). Focal seizures are triggered by a small group of neurons forming an epileptic focus, and depending on the site where it occurs, symptomatology is variable. The focal seizure usually consists of a multiplicity of signs, sequentially and simultaneously, reflecting the anatomo-functional circuitry involved in the onset and spread of the seizure.

Critical episodes are distinguished into focal with preserved awareness, originally defined as simple focal with impaired awareness originally defined as complex. In these crises, the subject's state of consciousness is not impaired.

According to Fisher, the subject retains awareness if he is aware of himself and his surroundings during the seizure, even if he remains immobile (6) of particular relevance is memory, if after the epileptic access the subject retains memory and recalls the event, the seizure is classified as focal in the absence of loss of awareness. Focal seizures are classified according to the predominant symptoms and signs at onset, which can be motor (focal seizures with motor onset) or non-motor (focal seizures with non-motor onset).

The most common motor signs are expressed as focal muscle contractions limited to a single body district, e.g., the hand, or may progressively recruit different ipsilateral districts, e.g., the hand, face, and tongue, an expression of the "Jacksonian march" that documents the involvement of several contiguous somatotopic regions in the motor cortex. Involvement of premotor cortical areas results in seizures with muscle contractions of the limbs and trunk.

Additional signs may involve lateral deviation of the head and eyes (versive seizures) due to involvement of the lateral frontal cortex, dysarthric seizures due to involvement of the opercular cortex or involvement of the supplementary motor area determine speech arrest, motor inhibition, and assuming specific postures. Also included are aggressive manifestations, eyelid blinks, manual automatisms, vocalization and verbal production (14). In focal seizures with non-motor onset, the manifestations are multiple and may affect thermoregulation, the cardiovascular and gastroenteric systems in the case of seizures with autonomic manifestations. In the case of cognitive seizures, the patient has the impression of having already experienced the current situation (dèJà vu), may experience a feeling of estrangement (jamais vu) or depersonalization. If the seizures are emotional or affective due to temporal and frontal lobe involvement, they are characterized by the sudden onset of emotion or manifest fits of laughter (gelastic seizures) and crying (dacristic seizures).

In somato-sensory focal seizures, the phenomenon is caused by the involvement of specific brain areas, involving hearing, smell and taste, sight, touch and balance. Auditory seizures are characterized by perception of simple and/or complex noises or distortion of sounds, suggesting involvement of the posterior portion of the superior temporal gyrus. Focal olfactory and gustatory seizures are characterized by gustatory illusions with involvement of the parietal operculum and olfactory with involvement of the basal frontal cortex. In visual seizures there may be altered shapes as well as scenes and may be present as scotomas or hemianopsia.

Somatosensitive seizures are responsible for tingling, pain, sensation of electrical discharge and a sense of drowsiness due to the involvement of the primary sensory area.

Vestibular focal seizures are rare and can be manifested by the impression of rotation of the external environment or as a displacement of the body in relation to the external environment, due to the involvement of the posterior temporal cortex and inferior parietal. In focal crises the first symptom defines the type of crisis, for example the diagnosis of crisis with impairment of awareness and automatisms is carried out if the first symptoms are motor. If during the crisis motor and non-motor symptoms occur, the motor signs are considered dominant, except if the dominant are the non-motor symptoms, for example sensory (6).

Generalized onset crisis: The generalized crises from onset were defined by Fisher as "originating in some point within, and with rapid commitment of bilaterally distributed networks", for the involvement of both cerebral hemispheres (6). Generalized motor seizures include tonic-clonic seizures, clonic seizures, tonic-clonic seizures, myoclonic seizures, myoclonic-tonic-clonic seizures, myoclonic-atonic seizures, atonic seizures and epileptic spasms. Among the generalized non-motor crises, we distinguish the palpebral absence, atypical absence and myoclonus.

Among the generalized motor crises are: Tonic-clonic crises are characterized by a first tonic phase, followed by the clonic phase and the postcritical phase. The crisis begins with a cry associated with loss of consciousness and sustained toning contraction of the muscles for 10-20 seconds.

In this first stage vegetative disorders include: changes in blood pressure, cardiac rhythm disturbances, salivary hypersecretion, pupil dilation associated with lateral tongue bite and cyanosis salivary hypersecretion, dilation of the pupil associated with lateral bite of the tongue and cyanosis of the face caused by apnea.

The clonic phase, characterized by bilateral and synchronous muscle contractions that progressively reduce frequency, lasts 30 seconds. In the post-critical phase, the subject may appear confused, is hypotonic and may follow post-critical sleep.

- Tonic crises are characterized by stiffening of agonist and antagonist muscles with muscle hypertone, associated with a brief alteration of the state of consciousness.
- Clonic seizures are characterized by rhythmic bilateral contractions of the striated muscles, which lead to convulsions in the subject, with loss of consciousness, in the context of rapid activity (10 Hz) and slow waves.
- Myoclonic crises are characterized by the appearance of an involuntary, short and sudden contraction of a muscle or group of muscles and appear in the absence

of alterations of the state of consciousness.

- Myoclonic-tonic-clonic seizures common in juvenile myoclonus epilepsy manifest with one or more myoclonic attacks on the limbs bilaterally followed by a tonic-clonic seizure.
- In myoclonic-atonic crises, myoclonic bursts are associated with an atonic component.
- Atonic seizures develop with a sudden loss of postural tone Neck, torso and limbs. Epileptic spasms are characterized by the flexion and/or extension of the proximal muscles and trunk.
- Spams are accompanied by eye movements and phenomena such as grimace and head nodding, head-like movements.

General non-motor crises include: Absences have a sudden beginning and end with a brief alteration of consciousness. The subject stops the activity and after a period of between 5 and 40 seconds resumes the activity. They are accompanied by myoclonic motor phenomena, the reduction of postural tone, gestures and vegetative signs.

Atypical absences have a longer duration than absences and a clinical picture characterized by motor components, often asymmetric, of tonic, atonic and myoclonus type.

The myoclonies of the eyelids last less than 10 seconds and are characterized by the upward deviation of the eyes and evoked by the closing of the eyes.

In crises with unknown onset, it is not possible to determine, on the basis of EEG characteristics, whether the crisis has a focal or generalized onset.

Within this category, motor crises are distinguished, in turn divided into tonic-clonic crises and epileptic spasms, and non-motor crises characterized by behavioral arrest. Finally, crises are defined as unclassified when the information is incomplete and there is no possibility to include them in the categories discussed above.

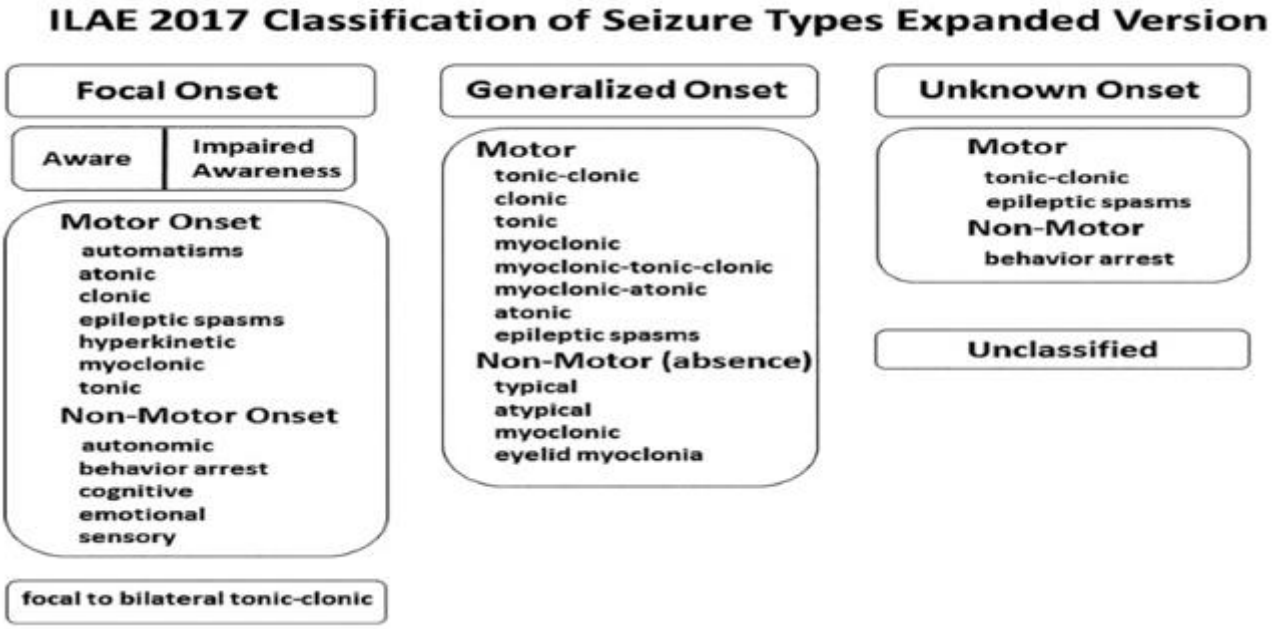

Figure 2: classification of crisis types in the extended version of 2017 (6).

The second level of classification: definition of the type of epilepsy

The second level of diagnosis, proposed by the International League Against Epilepsy, is aimed at defining the type of epilepsy and distinguishes between: focal, generalized, combined focal and generalized epilepsies and unknown epilepsies, further distinguished according to the specific etiology.

Focal epilepsies: Genetic focal epilepsies are characterized by the absence of cognitive and neurological deficits, often age-dependent with a favorable outcome to therapy. This category includes:

Benign rolandic tip epilepsy manifests itself, almost exclusively in sleep, with localized clones, dysarthria and hyperventilation.

Benign occipital epilepsy is characterized by vegetative, affective and/or visual symptoms. Among the visual symptoms, negative symptoms (transient loss of vision) or positive symptoms (visual hallucinations, phosphenes) expression of the parieto-occipital and temporal areas are distinguished.

Autosomal dominant nocturnal frontal lobe epilepsy is associated with nocturnal motor seizures, typically in the early hours of sleep or upon awakening, with dystonic/hyperkinetic manifestations and automatisms. They are associated with mutations in the CHRNA 4 and CHRNB2 genes.

Autosomal dominant lateral temporal lobe epilepsy with auditory symptoms is caused by a mutation in the LGI1 gene (on chromosome 10q24). Seizures are characterized by dysphasic manifestations, auditory, visual and less frequently psychic hallucinations.

Autosomal dominant familial temporal lobe epilepsy is characterized by vegetative, cognitive and emotional symptoms caused by the involvement of temporo-mesial structures.

In focal structural, metabolic, infectious and immune epilepsies, the presence of a brain lesion in the frontal, temporal, parietal or occipital lobe has been demonstrated and depending on the location of the lesion the symptomatology is variable.

An example of symptomatic focal syndrome is temporal lobe epilepsy associated with hippocampal sclerosis. It is a frequent focal syndrome in young adults and often drug-resistant, it arises in the limbic areas of the mesial temporal lobe (amygdala, hippocampus, para hippocampus) and can be associated with a triggering event such as prolonged and complex febrile seizures.

The main signs/symptoms include ascending epigastric sensation, déjà vu and déja vécu, fear, automatisms and dystonic postures. Other focal syndromes are elastic epilepsy, which arises with sudden and unmotivated laughter fits and Kojewnikov syndrome characterized by Jacksonian-type motor seizures and myoclonus of the upper limbs.

Generalized epilepsies

Onset in genetic generalized epilepsies usually originates in childhood and/or adolescence in the absence of neurological changes.

EEG shows bilateral and synchronous critical and intercritical abnormalities. The main forms of genetic generalized epilepsies are divided into:

Epilepsy absence of childhood, is the most frequent form of idiopathic generalized epilepsy of the developmental age. It begins after three years of age with a prevalence in women (60%). They are usually short-lived (5-10 seconds), multi-daily (up to 50-100 seizures/24 hours) with sudden onset and cessation (17). They are more frequent in the morning and are characterized by a sudden psychomotor arrest and loss of contact with the environment and a sudden resolution. Sometimes clonias, eyelid myoclonus and motor automatisms may be present and may be accompanied by absence of enuretic, pallor and redness of the face. The prognosis is favorable with a prompt response to drugs, such as valproic acid and ethosuccimide (17).

Absence epilepsy of adolescence has an onset between 10 and 17 years of age and the prognosis is more uncertain than in the infantile form. It manifests itself with absence seizures, rare myoclonus and generalized tonic-clonic seizures.

Juvenile myoclonic epilepsy (JME, from the Anglo-Saxon definition of Juvenile Myoclonic Epilepsy) or Janz syndrome, named after the epileptologist who first described its characteristics is one of the most frequent generalized idiopathic forms. From an epidemiological point of view, 1:1000 individuals suffer from it, representing about 10% of all epilepsies (18); it is equally distributed in both sexes and begins in puberty with a peak between 12 and 18 years of age, with bilateral, arrhythmic, single or repetitive myoclonic shocks, which can be the cause of a sudden fall for the patient (6).

Seizures are brief (<100 ms), arrhythmic, sudden, and involuntary, typically occurring after waking up, and precipitated by sleep deprivation. Since they are not accompanied by altered consciousness, they are often neglected and months or years can pass before a consultation (17).

Epilepsy with seizures of great mal upon awakening begins between the ages of 6 and 35, with a maximum peak at 18 years of age. It is characterized by generalized tonic-clonic seizures that occur mainly upon awakening.

Jeavons syndrome has a prevalence in the female gender and occurs between 2 and 14 years of age. The seizures are characterized by eyelid myoclonus and rare generalized tonic-clonic seizures. This category also includes: benign familial neonatal seizures, benign myoclonic epilepsy of the infant and epilepsies generated by specific modes of provocation (18).

Self-limited neonatal seizures and familial neonatal epilepsy (BFNE) differ in etiology, in neonatal seizures the mutations are de novo, a contrario in familial neonatal epilepsy (The syndromes arise between the fourth and seventh day of life during wakefulness and sleep, as focal seizures, which alternately affect both sides of the body and are often associated with apnea, begin with a tonic posture and progress with clonic movements with motor automatisms. The seizures are short-lived (1-2 minutes) with a daily frequency, up to 20 times, and can evolve into the state of evil. Newborns from a neurological and neurocognitive point of view are normal, only in some patients a slight learning difficulty has been found. If seizures occur in the first two months of life, beyond the neonatal period, epilepsy is identified as familial self-limiting neonatal-infantile epilepsy (19,20,21), BFNE is caused by mutations in the KCNQ2 and KCNQ3 genes, encoding voltage-gated potassium channel subunits (22).

The prognosis is favorable, the seizures tend to disappear spontaneously in the first year of life, but may continue after the year as occasional febrile seizures or idiopathic diseases of childhood. The classification developed by the International League Against Epilepsy included two new groups of epilepsy in the 2017 revision, "Combined Generalized and Focal Epilepsies" and "Epilepsy of Unknown Type". The need, in the first case, arises from some patients who have both generalized and focal seizures. Examples include Dravet syndrome and West syndrome, in which both types of seizures occur. In the second case of "Unknown Type Epilepsy" it is used in patients with epilepsy that cannot be ascribed within the existing categories, due for example to normal EEG and therefore not informative (18).

Dravet syndrome or acute myoclonic epilepsy of childhood, is one of the epileptic encephalopathies and begins in the first year of life in the normal child. Skull size and neurological examination are initially normal, later pyramidal signs and ataxia may occur. It is characterized by myoclonic and other seizures, including epileptic absences,

atonic and focal seizures. The syndrome does not involve tonic seizures and epileptic spasms. The attacks are resistant to treatment accompanied by developmental and cognitive decline. Antiepileptic drugs can aggravate seizures. West syndrome or epileptic encephalopathy with hypsarrhythmia, falls within the scope of epileptic encephalopathies and is characterized by the co-presence of infantile spasms. The peculiar feature of the syndrome is the flexion spasm that can involve the body in its entirety or the nape of the neck. It begins before one year of age and the incidence is higher for the male gender. Genetic factors include cortical dysgenesis (abnormal organ development), Bourneville's tuberous sclerosis and Aicardi's syndrome, caused by the mutation of the x chromosome, which causes agenesis (developmental arrest) of the corpus callosum. Genetic abnormalities associated with West Syndrome include: ARX, CDKL5, SPTAN1, STXBP1 and underlie structural brain abnormalities, e.g., TSC1 and TSC2 in tuberous sclerosis (23,24,25).

Third level of classification epileptic syndromes: the third level of classification organizes epilepsies into syndromes, based on clinical and electrical characteristics derived from EEG findings and neuroimaging.
The syndromes are distinguished by the age of onset, the type of seizure, the EEG characteristics, the coexistence of these factors allows the specific diagnosis of epilepsy syndrome to be reached. The diagnosis of the syndrome provides information on the etiologies to be examined and the pharmacological treatment to be adopted for the purpose of usefulness, as some epileptic drugs can aggravate seizures and early diagnosis can avoid drug treatment (International League Against Epilepsy, 2019).

The syndromes differ according to the time of onset into:
Neonatal syndromes: self-limited neonatal seizures and self-limited familial neonatal epilepsy, early myoclonic encephalopathy, Ohtahara syndrome, West syndrome, Dravet syndrome, myoclonic epilepsy of childhood, epilepsy of childhood with focal migratory seizures, myoclonic encephalopathy in non-progressive disorders, febrile seizures and genetic epilepsy with febrile seizures);
Syndromes of childhood: epilepsy with myoclonic-atonic seizures, epilepsy with eyelid myoclonus, Lennox-Gastaut syndrome, epilepsy of childhood absences, epilepsy with myoclonic absences, Panayiotopoulos syndrome, infantile occipital epilepsy, photosensitive occipital lobe epilepsy, infantile epilepsy with central temporal spikes, infantile atypical epilepsy, epileptic encephalopathy with continuous spikes and waves during sleep, Landau-Kleffner syndrome and epilepsy of the autosomal dominant nocturnal frontal lobe;
Adult/adolescent syndromes: juvenile epilepsy in absence, juvenile myoclonic epilepsy, epilepsy with isolated generalized tonic clonic seizures, autosomal dominant epilepsy with auditory features, other familial temporal lobe epilepsies;
Syndromes at any age: familial focal epilepsy with variable foci, reflex epilepsies, progressive myoclonic epilepsies;

Diagnosis: In order to make a diagnosis of epilepsy, two aspects must coexist: The finding of an epileptic seizure; and the tendency of the crisis to repeat itself. It is not justified to diagnose epilepsy in the presence of an isolated seizure (6) or in the case of epileptiform electroencephalographic changes not associated with seizures. The anamnestic investigation is the first step in formulating a precise and accurate diagnosis.

In the anamnestic collection, the goal is to obtain as much information as possible to define the type of seizure, identify any etiological and/or triggering factors, define the type of syndrome and its etiology and exclude critical events of a non-epileptic nature. Once the anamnestic-clinical investigation has been completed and the condition of the individual organs and systems has been assessed, the patient undergoes an electroencephalographic study to define the type of seizure and/or epileptic syndrome. The various types of EEG recording used for the diagnosis of patients with suspected or already established epilepsy are: routine EEG, Dynamic EEG or 24-hour EEG, EEG with Video Recording and long-term Video-EEG monitoring. Routine EEG recording involves recording in baseline conditions (eyes closed and open) for at least 20 minutes. In 10-20% of patients with epilepsy, a normal trace can be observed and in case of normality of the trace, activation methods such as hyperventilation, intermittent light photo stimulation, recording during spontaneous sleep or night sleep deprivation will be implemented, subsequently once the diagnosis of Epilepsy has been made, the EEG is repeated. Diagnostics are completed by morphological neuroimaging and functional neuroimaging. Brain magnetic resonance imaging (MRI), and less useful computed tomography (CT), are an essential element in the diagnostic approach. Magnetic resonance imaging contributes to the etiological diagnosis by identifying possible pathologies underlying epilepsy. Functional neuroimaging makes use of tests such as Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography (PET), Magnetic Resonance Spectroscopy (MRS) and Functional Magnetic Resonance Imaging (FRMI), which allow the evaluation of alterations in the structures affected by epileptic processes. Neuropsychological assessment is aimed at assessing the patient's cognitive level and individual skills in specific tasks, it is of particular relevance in developmental age and during pre-surgical study (6). Psychological assistance is useful for reducing the psychological impact that the diagnosis entails and is important in the comparison between the starting situation and the next one

Neuropsychological evaluation in patients with epilepsy
The neuropsychological assessment is carried out, in clinical practice, by the neuropsychologist, who has the task of formulating diagnostic hypotheses to select the tools aimed at examining cognitive processes and verifying the diagnostic hypothesis. Assessment consists of several phases: the clinical interview with the patient, the evaluation of the neuropsychological history, the behavioral evaluation, the functional evaluation and the administration of appropriate neuropsychological tests with the assessment. The choice of assessment methods depends on numerous variables: the nature of the symptoms and pathology, the severity of the damage, the age of the

examinee, the setting or context of the assessment and the specific objectives of the assessment.

Neuropsychological evaluation with epileptic patients aims to:

1. Identify, describe and interpret cognitive dysfunctions and/or deficits;
2. Detect the patient's cognitive potential and reserves;
3. Contribute to the differential diagnosis of neuropsychiatric and/or neurodevelopmental disorders;
4. Detect the neurobehavioral consequences of psychopharmacological interventions;
5. Determine a starting point and make a prognosis regarding the evolution of neuropsychological deficits;
6. Establishment of an individualized rehabilitation program based on the knowledge of limitations, but also of preserved abilities, which allows to optimize autonomous functioning and improve the patient's quality of life.

Between the patient and the specialist, it is functional that a bond of trust is created, which is essential for the validity of the measurements, which also seem to be affected by the effect of motivation (26).

In this evaluation process, it is customary to carry out a comprehensive assessment of all cognitive, behavioral and emotional aspects of the patients to avoid distorted interpretations of the results obtained. To do this, quantitative measures, mainly standardized tests, as well as qualitative measures must be used together. The latter derive from the neuropsychologist's observation of the way in which the person performs these tests, i.e. the process and not exclusively the result. Given that most neuropsychological tests are multifactorial, meaning they involve various cognitive processes, focusing solely on the final score on a given test and ignoring how the person solves it, would reduce the interpretive power of neuropsychological tests. Since cognitive functions are correlated, by focusing attention on the process and not on the result, it is possible to determine to what extent a function can interfere with the execution of a given task that in principle is intended to measure a different function.

Thus, for example, a person may fail in verbal episodic memory tasks if he has so much difficulty avoiding distractors (selective attention) that he cannot encode the information provided, so he will not even be able to memorize and retrieve it later. In this case, only if we can eliminate the artifact that is distraction, can we talk about that patient's episodic memory capacity. The same thing usually happens in those tests where the correction is performed as per its resolution in a predetermined time. If we allow the person to use the necessary time, it is possible to discriminate between the deterioration of the function to complete that task and the presence of a slowed processing and execution speed.

On the other hand, it is convenient to collect information on the impact that neuropsychological alterations produce on the functional independence and psychosocial adaptation of the person.

These functional assessments, usually consisting of questionnaires with parallel modules for the patient and family, allow to evaluate the performance in a specific task and situation, which facilitates the inference about the person's real ability in daily activities, giving it greater ecological validity.

The patient's performance is assessed by analyzing the results of the tasks administered, expressed in the form of a score and then compared with the normative scores relating to age and level of education.

The neuropsychological assessment is therefore not a mechanistic procedure, but on the contrary must be adapted to the patient's clinical history, taking into consideration psychological, social, cultural, family, demographic, cognitive, developmental, neuromorphological, neurophysiological and pharmacological parameters.

The evaluation must be multi-component and consider the patient from a psychological perspective, as well as a strictly neuropsychological one, also considering the patient's emotional reactions. The evaluation is distinguished between patients who respond to pharmacological treatment and patients who are candidates for surgical therapy due to drug resistance.

In the case of patients who respond to drugs, and therefore are not candidates for surgical therapy, the neuropsychological evaluation aims to detect the patient's cognitive abilities and cognitive disorders by defining a neurobehavioral profile and designing an individualized neurocognitive rehabilitation plan. In patients with drug-resistant epilepsy, the objective of the evaluation is to detect cognitive deficits and identify the underlying neuroanatomical substrate by demarcating the area of functional deficit, i.e. the areas that present dysfunction during the interictal period.

The examination in drug-resistant patients combines localization information with information from preoperative monitoring examinations to highlight the brain areas of interest.

The combination of these measures allows the neuropsychologist to obtain a global view of the functioning of the evaluated subject.

The neuropsychological evaluation must be as complete as possible by examining the main cognitive functions: executive functions, visual-spatial skills, memory and learning and language.

The MMSE consists of thirty items that assess orientation, short and long-term memory, language, attention, visuospatial skills, and the ability to follow simple verbal and written commands. This easy-to-use and relatively quick neuropsychological test is often employed to assess the overall cognitive status (27).

The main neuropsychological tests used to assess cognitive functions include:

Stroop Color- Word Test: is a neuropsychological test that assesses the capacity for selective attention and the components of executive functions such as cognitive flexibility and the ability to inhibit interfering or irrelevant stimuli (28,29).

Trail Making Test (TMT): it is a neuropsychological test aimed at assessing attention skills, with particular reference to planning, visual-motor speed and cognitive flexibility,

The Trail Making Test (TMT) measures visual attention and task switching. It consists of 25 circles distributed over a sheet of paper.

In part A, the circles are numbered from 1 to 25, and the patient should draw lines to connect the numbers in ascending order. The patient is instructed to connect the circles as quickly as possible without lifting the pen or pencil from the paper. The time to connect the "trail" is measured. If the patient makes an error, the examiner immediately points it out to allow the patient to correct it. Errors affect the patient's score as the error correction is included in the time completion for the task. The test is interrupted if the patient has not completed both parts within five minutes (30).

Memory: The Babcock Story Recall Test (BSRT) measures immediate and delayed recall. The examiner reads a brief story, and the participant must provide immediate recall.

Then, the story is repeated, and a delayed recall is obtained after ten minutes (31).

The Serial Repetition Test of Two-syllable Words measures verbal short-term memory. In this test, the examiner presents a sequence of unrelated two-syllable words that the subject must repeat immediately after the presentation. The test is preceded by an example. The examiner begins with a two-word sequence; if the subject correctly repeats 2 out of 3 stimuli, the examiner moves to a longer set (one more word). The span is given by the longest sequence for which at least 2 out of 3 stimuli are correctly repeated (32).

Language: The Verbal Fluency Test is a short test of linguistic functioning (33,34). It consists of two tasks: category or semantic fluency and letter or phonemic fluency. Semantic verbal fluency is measured by the number of words produced within a restricted category. Name categories are semantic colors, animals, and fruits. Concerning phonemic fluency, participants were instructed to generate words beginning with the test letters F, A, and S, spelled out loud by the examiner in this order. Examinees were given 60 s to name as many words as possible, beginning with the first letter; the procedure was then repeated for the two remaining letters. The participants were informed of inadmissible words (repetitions, proper names, or words with different inflections sharing the same root) to be eliminated from the analysis. Application and scoring criteria were derived from Senhorini et al. (35). Instructions were followed by examples using the letter P to illustrate correct and incorrect words. The participants are given 1 min to produce as many unique words as possible within a semantic category (category fluency) or starting with a given letter (letter fluency). The participant's score in each task is the number of unique correct words.

Constructional praxis: The Constructional Apraxia Test (CAT) (36,37) was used to measure the ability to consistently copy the elements that constitute the geometric bidimen-sional models presented by the examiner. The figures derive from those used in the test of Arrigoni and De Renzi (38). After the run-in, the examiner presents the figures printed on the upper half of the paper; the participant is asked to copy them below as precisely as possible. A score of 4 is given if the reproduction is perfect, 1 if the copy is partially defective, and 0 if the reproduction is unrecognizable or if there is a "closing-in" (despite the instructions, the subject follows the contour of the figure printed above).

Fluid Intelligence: The Raven's Coloured Progressive Matrices (CPM) (39) is a non-verbal intelligence test representative of general intellectual capacity or the "g" factor proposed by Spearman. The CPM was developed to assess children aged from 5 to 11 years old, mentally disabled individuals as well as older individuals. The items are organized in ascending difficulty throughout three sets (A, Ab, and B). On average, set B is more difficult than set Ab, which is more difficult than set A. The items consist of a drawing with a missing part, which the individual needs to complete by choosing one among six alternative responses. There is only one correct answer for each item. The respondents score one for each correct response and zero for each wrong response. The minimum score is 0, and the maximum score is 36.

Visual-spatial skills: Visual-spatial skills consist of the ability to integrate information from perceptual space to develop spatial coordinates that allow the proposed material to be organized and used to adequately perform a task. A neuropsychological test frequently used to assess visual-spatial skills is: Rey's Figure Test: the neuropsychological test assesses visual-constructive spatial skills, planning, organizational skills and problem-solving strategies. (40).

Course tests: or tests for visuospatial MBT Corsi's Block Tapping Test measures visuospatial working memory. This test consists of nine cubes fastened in random order to a blackboard; each time the examiner taps the blocks in a prearranged sequence, the patient must copy the tapping pattern, which involves a series of blocks of increasing span length to be tapped by the patient in a forward (memory span) or backward (working memory span) manner (41).

Neuropsychological intervention

The neuropsychologist, after documenting the patient's cognitive and behavioral deficits, proceeds to plan a rehabilitation program planned on the needs of each individual with the ultimate goal of functional recovery of the affected areas. In cases of severe impairment of brain tissue, compensatory strategies are adopted, which recruit new areas and replace the compromised ones, in this case we speak of functional replacement rather than functional recovery.

In functional replacement, functionally intact areas perform tasks normally performed by damaged areas.
Ponds, identified the three central aspects of neuropsychological intervention:

- Psycho-education to the effects of brain damage in a realistic perspective and cognitive difficulties;
- The impact of personality changes and emotional reactions;
- individual perception of cognitive disorders;

In reference to personality changes, these include behavioral problems (impulsivity and low tolerance for frustration), lack of understanding (and consequently poor motivation), symptoms of depression and anxiety, acceptance problems, personality traits such as neuroticism, rigidity or compulsiveness, and dysfunctional thought patterns such as catastrophic reactions or the desire that only returning to the situation before the deficit can be satisfying.

These problems strongly interfere with learning and should therefore be taken into account before rehabilitation begins. In addition, for some patients there is a large discrepancy between the severity of memory impairments observed as indicated with memory tests and the severity and impact of these memory problems in daily life.

With reference to the individual perception of cognitive disorders, it emerges that the beliefs and perceptions that the patient holds about his memory strongly influence the activities in which he will engage or how he will perform a memory task. If these memory beliefs are deficient, it is very likely that the patient will invest less effort (or inefficient allocation of effort) into daily memory tasks, which could lead to lower memory performance.

The more specific aspects of the program have to do with:

- what memory problems should be trained;
- what are the best strategies to use;

Memory training must be differentiated from subject to subject and the objectives must be built together with the patient.

For example, "general improvement of memory to the level it was before my accident" is not a good training goal, but learning the names of nursing staff may be. The goals should always be tailor-made, small, as concrete as possible and fully tailored to the patient's needs and wishes.

Of course, it is possible to learn a general strategy for remembering names, but only after repeated practice will the patient generalize this strategy to other "name situations" than the one for which he or she was trained.

As a general rule, it could be said that patients alone have a lot of difficulty applying learned strategies beyond the training situation or beyond the training period. Most memory patients share many common memory problems.

The main methods of neuropsychological memory rehabilitation in patients with epilepsy are:

- The development of strategies (relearning);
- Repetition of cognitive tasks (re-education);
- Use of external aids;
- Error-free learning;

Cognitive support: Mnemontechnics;
Strategizing (relearning) involves the use of verbal strategies, such as depth of information encoding, processing, and recall through the use of cues. In relation to relearning, recent studies have shown that patients with left temporal lobe epilepsy benefit from strategies such as semantic processing and coding, while patients with right temporal epilepsy would benefit from cue-based recall.

The second method, the repetition of cognitive tasks (re-education) is based on the learning of mnemonic rules, such as: "choosing and organizing information strengthens memory", "greater intervals of learning seem to improve memory" and "repetition improves memory". Errorless learning aims to reduce errors during the mnestic coding phase of the information being learned, facilitating correct answers.

Cognitive support (scaffolding) aims to bridge the gap between what can be achieved independently and the goal to be achieved.

The technique must offer patients support or support from the operator, control and autonomy, feedback and metacognitive training based on the representation of information (graphs, images and simulations). Finally, mnemonics, strategies and techniques used to promote learning, aim to enhance the processes of storing information. Mnemonics include: mental imagery which induces the patient to create and store images containing verbal information, recalled in the form of images; verbal elaboration which, through associations, facilitates the mnestic coding and the method of loci. Recently, rehabilitation approaches defined as "ecological", which simulate everyday life situations, have also been adopted with epileptic patients. Yang and collaborators used simulations as a rehabilitation tool in 2010. During the simulations, the patient simulated driving the car while electroencephalographic activity was recorded to study the triggering of seizures caused, for example, by driving and lay the foundations for a rehabilitation path. In general, the memory deficits seen in patients with epilepsy are less severe than in severely brain-damaged patients or those with dementia or Korsakoff syndrome. In addition, unlike, for example, patients with frontal lobe damage or those with specific neuropsychological disorders such as anosognosia, patients with epilepsy generally retain sufficient insight into their daily possibilities and deficits.

In addition, since epilepsy is a chronic disease, it is possible to assume that memory problems will worsen over time. A final aspect to consider in the design of the intervention is that during a memory treatment seizures can also interfere with progress or cause temporary interruption of treatment.

Cognitive rehabilitation has been applied to treat patients with epilepsy in the last decade with the aim of compensating for impaired functions, improving the patient's quality of life and strengthening residual abilities. Studies have shown that the pathophysiological and clinical

characteristics of the disorder can provide specific indications for the structuring of rehabilitation programs.

Cognitive rehabilitation programs that use compensatory strategies and a holistic approach that includes: cognitive exercises specifically training for visual or verbal memory and attention, group therapy aimed at psychoeducation and the teaching of compensatory strategies, occupational therapy and sociotherapy are effective.

The holistic approach, compared to the single technique, has the advantage of simultaneously addressing the cognitive and behavioral problems that cause psychosocial disabilities. In addition, the studies in the literature converge in considering the personalization of the rehabilitation intervention and the therapeutic alliance between the patient and the staff central in order to obtain good results.

Conclusion

The results of neuropsychological assessment can be used to create a tailor-made rehabilitation program to reduce the impact of any cognitive deficits.

Memory problems, difficulties with concentration and executive dysfunction are often an integral of the condition, seizures and cognitive difficulties are both a manifestation of brain pathology. The cognitive problems associated with the pathology are exacerbated by the treatments aimed at reducing the seizures. Many people with epilepsy report that these aspects of their condition have never been explained to them. People with epilepsy should feel comfortable in whatever context they find themselves, without the fear of being ostracized for their condition.

Stigma is the biggest problem for people who develop epilepsy; for many people with epilepsy, the stigma itself is more disturbing than managing the clinical effects of the disease. The more evident the stigma, the more discriminatory, concrete and tangible it is and frequently pushes the people who are recipients of it and their families to live the disease with discomfort, shame and often isolating themselves.

The effects of stigma are debilitating and affect many areas of life for people with epilepsy, including difficulties accessing education, finding and maintaining stable employment, and/or developing intimate relationships.

They have the right to live their lives without being constantly dependent on their caregiver, knowing that they are safe outside their care.

The multi-component intervention aims to consider the patient from a psychological perspective, as well as a strictly neuropsychological one, also considering the patient's emotional reactions.

References

1. Gowers WR (1881) Epilepsy and other chronic convulsive disorders. Churchill, London.
2. Trimble MR. Cognitive hazards of seizure disorders. Epilepsia 1988;29 (Suppl.1):S19–24.
3. Bumke O. Die Diagnose der Geisteskrankheiten. Wiesbaden: Verlag von F.J. Bergmann; 1919.
4. Wildermuth HA. Zeitschrift f. d. Behandlung Schwachsinniger und Epileptiker.Dresden/Druck Johannes Pässler, Dresden: Warnatz nigl. Hofbuchhändler; 1897.
5. Fisher RS, Cross JH, French JA (2017) Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. Epilepsia, 58, 522-530.
6. Fisher, S. R., Cross, H. J., D'Souza, C., French, J.A., Haut. S.R., Higurashi, N. et al. (2017). Instruction manual for the ILAE 2007 operational classifictaion of seizure types. Epilepsia, 58, 531-542
7. Kotsopoulos, I. A., van Merode, T., Kessels, F. G., de Krom, M. C., & Knottnerus, J. A. (2002). Systematic review and meta-analysis of incidence studies of epilepsy and unprovoked seizures. Epilepsia, 43(11), 1402–1409
8. Muayqil, T. A., Alanazy, M. H., Almalak, H. M., Alsalman, H. K., Abdulfattah, F. W., Aldraihem, A. I., Al-Hussain, F., & Aljafen, B. N. (2018). Accuracy of seizure semiology obtained from first-time seizure witnesses. BMC neurology, 18(1), 135
9. Mecarelli, O., Messina, P., Capovilla, G., Michelucci, R., Romeo, A., Beghi, E., & Epischool Collaborative Group of the Lega Italiana contro l'Epilessia (LICE) (2014). An educational campaign toward epilepsy among Italian primary school teachers: 1. Survey on knowledge and attitudes. Epilepsy & behavior: E&B, 32, 84–91.
10. Savarese, G., Carpinelli, L., D'Elia, D., & Coppola, G. (2015). Teachers of various school grades and representations of epilepsy: problems, relational aspects and perspectives of life quality. Italian journal of pediatrics, 41, 70.
11. Lega italiana contro l'epilessia [LICE]. (2021). "A scuola di epilessia, quando la malattia ci chiede di sapere": online la prima campagna educativa digitale nelle scuole promossa dalla LICE. https://www.lice.it/LICE_ita/comunicati_ufficiali/pdf/160321_Comunicato_LICE_Campagna_Educativa_Scuole.pdf
12. LICE. & Società italiana di medicina generale [SIMG]. (n.d.). Guida pratica per la gestione del paziente affetto da epilessia [Brochure]. https://lice.it/LICE_ita/documenti_LICE-SIMG/pdf/1_clinica.pdf
13. Netter H. (2014) Atlante di anatomia Fisopatologica e Clinica, Edra.
14. Berardelli, A. (2019) La neurologia della sapienza, Società Editrice Esculapio, Bologna.
15. Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for classification of epilepsies and epileptic syndromes. Epilepsia 1985;26: 268- 278.
16. The International League Against Epilepsy (ILAE), Epilepsia, 58(4):512–521, 2017 doi: 10.1111/epi.13709
17. Matricardi S, Verrotti A, Chiarelli F, Cerminara C, Curatolo P. Current advances in childhood absence epilepsy, Pediatric Neurology, 2014
18. Scheffer I, Berkovic S et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for

Classification and Terminology. Epilepsia, 2017; 58(4): 512–521. doi: 0.1111/epi.13709
19. Clancy RR, Legido A. The exact ictal and interictal duration of electroencephalographic neonatal seizures, Epilepsia 1987;28:537.
20. Scher MS, Aso K, Beggarly ME, Hamid MY, Steppe DA, Painter MJ. Electrographic seizures in preterm and full-term neonates: clinical correlates, associated brain lesions, and risk for neurologic sequelae. Pediatrics 1993b;91: 128.
21. Scher MS, Alvin J, Gaus L, Minnigh B, Painter MJ. Uncoupling of EEG-clinical neonatal seizures after antiepileptic drug use. Pediatr Neurol 2003;28: 277-80
22. Zara F, Specchio N, Striano P, et al. Genetic testing in benign familial epilepsies of the first year of life: clinical and diagnostic significance. Epilepsia 2013;54: 425–436.
23. Pavone P, Spalice A, Polizzi A, et al. Ohtahara syndrome with emphasis on recent genetic discovery. Brain Dev 2012;34: 459–68.
24. Kato M, Yamagata T, Kubota M, et al. Clinical spectrum of early onset epileptic encephalopathies caused by KCNQ2 mutation. Epilepsia 2013; 54:1282–1287.
25. Saitsu H, Kato M, Koide A, et al. Whole exome sequencing identifies KCNQ2 mutations in Ohtahara syndrome. Ann Neurol 2012;72: 298-300
26. Stylianos G., Lucci G., Panayiotis P (2019). La neuropsicologia dell'epilessia: Aspetti neurocognitivi e comportamentali della malattia sacra, Franco Angeli, Milano.
27. Tombaugh, T.N.; McIntyre, N.J. The mini-mental state examination: A comprehensive review. J. Am. Geriatr. Soc. 1992, 40, 922–935
28. Stroop J. (1985). Studies of interference in serial verbal reactions. J Exp Psychol 18,643-62.
29. Strauss E., Sherman E., Spreen O. (2006). A Compendium of Neuropsychological Sghirlanozni,A. (2014) Terapie delle malattie neurologiche, Springer-Verlag, Italia. Tests: Administration, Norms, and Commentary. Oxford University Press.
30. Giovagnoli, A.R.; Del Pesce, M.; Mascheroni, S.; Simoncelli, M.; Laiacona, M.; Capitani, E. Trail making test: Normative values from 287 normal adult controls. Ital. J. Neurol. Sci. 1996, 17, 305–309
31. Babcock, H.; Levy, L. Test and Manual of Directions; The Revised Examination for the Measurement of Efficiency of Mental Functioning; Stoelting: Wood Dale, IL, USA, 1940.
32. Spinnler, H.; Tognoni, G. (Eds.) Standardizzazione e Taratura Italiana di Test Neuropsicologici. Ital. J. Neurol. Sci. 1987, 8 (Suppl.6), 20–120
33. Caltagirone, C.; Gainotti, G.; Carlesimo, G.A.; Parnetti, L.; e il Gruppo per la standardizzazione della batteria per il deterioramento mentale. Batteria per la valutazione del deterioramento mentale (Parte I): Descrizione di uno strumento di diagnosi neuropsicologica. Arch. Psicol. Neurol. Psichiatr. 1995, 56, 461–470.
34. Carlesimo, G.A.; Caltagirone, C.; Gainotti, G.; Fadda, L.; Gallassi, R.; Lorusso, S.; Marfia, G.; Marra, C.; Nocentini, U.; Parnetti, L. The mental deterioration battery: Normative data, diagnostic reliability and qualitative analyses of cognitive impairment. Eur.Neurol. 1996, 36, 378–384
35. Senhorini, M.C.; Amaro Júnior, E.; de Mello Ayres, A.; De Simone, A.; Busatto, G.F. Phonemic fluency in Portuguese-speaking subjects in Brazil: Ranking of letters. J. Clin. Exp. Neuropsychol. 2006, 28, 1191–1200
36. Carlesimo, G.A.; Caltagirone, C.; Gainotti, G.; Nocentini, U.; e il Gruppo per la Standardizzazione della batteria per il deterioramento mentale. Batteria per la valutazione del deterioramento mentale (Parte II): Standardizzazione e affidabilità diagnostica nell'identificazione dei pazienti affetti da sindrome demenziale. Arch. Psicol. Neurol. Psichiatr. 1995, 56, 471–488.
37. Carlesimo, G.A.; Caltagirone, C.; Gainotti, G.; Fadda, L.; Gallassi, R.; Lorusso, S.; Marfia, G.; Marra, C.; Nocentini, U.; Parnetti, L. The mental deterioration battery: Normative data, diagnostic reliability and qualitative analyses of cognitive impairment. Eur.Neurol. 1996, 36, 378–384
38. Arrigoni, G.; De Renzi, E. Constructional apraxia and hemispheric locus of lesion. Cortex 1964, 1, 170–197
39. Basso, A.; Capitani, E.; Laiacona, M. Raven's Coloured Progressive Matrices: Normative values on 305 adult normal controls. Funct. Neurol. 1987, 2, 189–194
40. Caffarra et. Al. 2000 The Rey Osterrieth Complex Figure. Neurol Sci 2002 Mar;22(6):443-7
41. Spinnler H.; e Tognoni G. (Eds.) Standardizzazione e Taratura Italiana di Test Neuropsicologici. Ital. J. Neurol. Sci. 1987, 8 (Suppl. 6), 20-120.