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A Review on Social-Economic and Epidemiology of Epilepsy

[1]Nkeiruka Chinedu-Anunaso, [2]A. O. Ogunrin, [2]F. A. Imarhiagbe and [2]F. Odiase

[1]Consultant Physician/Neurologist Internal Medicine Department
Federal Medical Centre Owerri.
[2]Consultant Physician/Neurologist, Department of Internal Medicine, University of Benin Teaching Hospital, Benin City Edo State Nigeria.

ABSTRACT

Epilepsy is the occurrence of two or more unprovoked seizures separated by at least 24 hours but multiple seizures occurring in a 24-hour period are considered a single event thus an episode of status epilepticus is considered a single event. Epilepsy has remained a major public health issue worldwide especially in developing African countries like Nigeria. It is the most common non-infectious neurologic disease in developing African countries including Nigeria and it remains a major medical and social problem. Epilepsy has significant economic implications in terms of health care needs, premature death and lost work productivity. An Indian study calculated that the cost per patient of epilepsy treatment was as high as 88.2% of the country's per capita Gross National Product (GNP), and epilepsy-related costs, which included medical costs, travel, and lost work time, exceeded $2.6 billion/year. The signs and symptoms of seizures vary and depend on where in the brain the disturbance first starts, and how far it spreads. Temporary symptoms occur, such as loss of awareness or consciousness, and disturbances of movement, sensation (including vision, hearing and taste), mood, or other cognitive functions. Epilepsy can be treated with a daily medication that costs as much as US$ 5 (1,800 Naira) per month. Recent studies in both low- and middle-income countries have shown that up to 70% of children and adults with epilepsy can be successfully treated (i.e. their seizures completely controlled) with anti-epileptic drugs (AEDs). In conclusion Idiopathic epilepsy is not preventable. However, preventive measures can be applied to the known causes of secondary epilepsy.
Keywords: Epilepsy, Social-Economic, Epidemiology and seizures

INTRODUCTION

Epilepsy is seen as a disease rather than a disorder. A seizure is an event while epilepsy is the disease associated with spontaneously recurrent seizures [1].The classification of seizures was recently reviewed by the International League against Epilepsy (ILAE) [2, 3]. Seizure is a transient occurrence of signs and or symptoms due to abnormal excessive or synchronous neuronal activity of the brain [4]. Seizures are typically paroxysmal and episodic, resulting in a suddenly occurring but transient behavioural, somatosensory, motor or visual symptoms and signs and caused by abnormally excessive cortical neuronal activity [5]. Seizures may be provoked by certain influences like trauma, brain haemorrhage, metabolic dyscrasias or drug exposure or occur simultaneously without provocation [6]. Some people with provoked seizures may have recurrent seizures without having epilepsy. Provoked seizures do not recur when provoking factors are removed [7]. A seizure is an event while epilepsy is the disease associated with spontaneously recurring seizures [8]. In reflex epilepsy for example photosensitive epilepsy, eating epilepsy, seizures are provoked but they are considered epilepsy because if the seizure threshold was not attained, these precipitants would typically not cause seizures [9]. Seizures can be caused by head injuries, brain tumors, lead poisoning, mal-development of the brain, genetic and infectious illnesses as well as fevers [10]. Epilepsy is a chronic disorder, the hallmark of which is recurrent, unprovoked seizures [11]. It is defined as a disease with either recurrent seizures (i.e. 2 or more unprovoked seizures occurring at least 24 hours apart) or a heightened tendency towards recurrent seizures (i.e. a single seizure accompanied by evidence that a heightened risk for

future seizures exists) or when an epilepsy syndrome is diagnosed [12]. This is the operational definition however there is a conceptual definition which defines epilepsy as a chronic disease of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological, and social consequences of this condition [13]. Cortical hyperexcitability, neuronal hypersynchrony and excessive neuronal excitation are all expression of epileptic predisposition. Gene mutation, channelopathies and receptor alterations are molecular levels of epileptic condition [14]. Epilepsy is the occurrence of two or more unprovoked seizures separated by at least 24 hours but multiple seizures occurring in a 24-hour period are considered a single event thus an episode of status epilepticus is considered a single event [15]. Febrile seizures or only neonatal seizures are not considered to be epilepsy [16].

A prevalent case of active epilepsy is defined as a person with epilepsy who has had at least one epileptic seizure in the previous 5 years, regardless of antiepileptic drug (AED) treatment [17, 18, 19]. Epilepsy in remission with treatment is a prevalent case of epilepsy with no seizures for ≥ 5 years and currently receiving AED treatment [20, 21, 22]. Resolved epilepsy is when an age dependent syndrome is outgrown or when a person is seizure free for at least 10 years, the last 5 years off anti-seizure medications [23]. Epilepsy is the commonest neurological disorder encountered in neurological practice [24]. It is estimated that it affects 50 million worldwide people, with higher incidence and prevalence figures in developing countries especially sub-Saharan Africa where the exact statistics are not available [25]. The prevalence and incidence figures available in the literature from sub-Saharan Africa are 'tips of iceberg [26]. The high treatment gap in sub-Saharan African countries implies that most patients with epilepsy (PWEs) are untreated [27]. This calls for studies to evaluate the effect of epilepsy on the cognitive functioning or performance of affected individuals.

Cognition comes from the Latin root *cognoscere*, which means "to know". It usually refers to everything that is related to knowledge. It can also be referred to as the accumulation of information acquired through learning or experience [30]. The most accepted definition of cognition is the ability to process information though perception, knowledge acquired through experience, and subjective characteristics that allow the integration all of the information, to evaluate and interpret the world [31]. Cognition is the ability to assimilate and process the information received from different sources (perception, experience, beliefs) to convert them into knowledge [32]. Cognition includes different cognitive processes, like learning, attention, memory, language, reasoning, decision making [33]. Cognitive processes are the procedures used to incorporate new knowledge and make decisions based on the knowledge[34].Different cognitivefuncti ons playaroleinthese processes: perception, attention, memory and reasoning. Each of these cognitive functions works together to integrate the new knowledge and create an interpretation of the world. In epilepsy, some of these cognitive processes are affected thereby making the patients to manifest with some forms of cognitive deficits [35]. Several relationships have been obtained between cognitive impairment and epilepsy-related or treatment-related factors [36]. One of these factors is treatment-related: the central cognitive side effects of the antiepileptic drugs (AEDs) [37]. The second and third factors are disease-related factors; the effect of the seizures and underlying epileptiform discharges in the brain and the localization of the epileptogenic focus in specific areas of the brain [38]. Although most cognitive problems have a multifactorial origin and often several factors combined are responsible for the cognitive problem, an attempt has been made to isolate one factor; the effect of seizures and epileptiform EEG discharges on cognitive function [39].

There are some risk factors that have been associated with cognitive deterioration in epilepsy. These include;

- Duration of epilepsy: Longer duration of epilepsy has been

reported to be associated with greater cognitive impairment. The negative impact of duration may be in part due to the cumulative impact of seizures, but also to other factors including antiepileptic drug (AED) treatment and pathologic interictal brain activity [40].

- Age of onset of seizure: An early age of onset is a risk factor for cognitive decline, as brains are less able to develop a functional reserve capacity to cope with subsequent loss. Advancing age, conversely, has been proposed as increasing the risk of cognitive decline, because having epilepsy accelerates the cognitive aging process [41].
- Duration between the onset of seizure and diagnosis/commencement of medications: Late diagnosis and commencement of medications have been found to increase the risk of cognitive decline. Clinical studies showed that cognitive impairments induced by seizures are reversible for most seizure types when seizures are diagnosed early and controlled adequately [42].
- Type of seizure: The risk of cognitive impairment is increased in some seizure types such as focal to bilateral tonic-clonic [43].
- Frequency and Duration of seizure: Cognitive decline has been recognized as a sequel of intractable epilepsy. A number of factors have been identified as having a role, including underlying pathology, seizures and medications. Status epilepticus and frequent recurrent chemically and electrically induced seizures can result in cognitive impairment. In individuals with high seizure frequency, cognitive impairment may have a greater impact on daily life [44].
- Type, dosage, duration and compliance of antiepileptic drugs: Antiepileptic drugs (AEDs), which not only reduce neuronal irritability but may also impair neuronal excitability. The major cognitive effects of AEDs are impaired attention, vigilance, and psychomotor speed, but secondary effects on other cognitive functions can be seen. AED-induced cognitive side effects are increased with rapid initiation, higher dosages and polytherapy [45].

Epilepsy commonly produce changes in cognitive abilities and may even manifest with neuropsychiatric symptoms [46]. The knowledge of the presence and characteristics of these cognitive disturbances can aid in the diagnosis, management and long term care of affected person [47]. Neuropsychological evaluation is one of the methods of garnering quantitative information about cognitive and behavioural changes in patients with known neurological diseases like epilepsy or who are considered to be at risk of brain dysfunction [48].

EPIDEMIOLOGY OF EPILEPSY

Epilepsy has remained a major public health issue worldwide especially in developing African countries like Nigeria [49]. It is the most common non-infectious neurologic disease in developing African countries including Nigeria and it remains a major medical and social problem [50]. At a conservative estimate, 50 million people worldwide have epilepsy with an annual incidence ranging from 20 to 70 cases per 100,000 and the point prevalence of 0.4 to 0.8 percent [51]. The incidence rates are highest in childhood, plateaus from the age of 15 to 16years, and rise again among the elderly [52]. Most patients suffering from epilepsy in African countries prefer anonymity and are reluctant to disclose their condition because of the stigma attached to the disease [53]. This factor affects the prevalence rates hence there is likelihood that most of the reported prevalence rates represent a `tip of the ice-berg' as the chances of under-reporting are high [54]. The prevalence rates of epilepsy reported in Africa are based on surveys of defined communities and hospital admissions [55]. The prevalence of epilepsy is particularly high in developing countries especially in Latin America

and several African countries, notably Liberia, Nigeria and United Republic of Tanzania, compared with the prevalence rates of between 4 and 6 per 1000 which have been reported among Caucasians [56].

In Nigeria, its prevalence, based on defined communities, varies from 15 to 37 per 1000. One of the early publications on the prevalence of epilepsy in Nigeria reported a prevalence of between 8 and 13 per 1000 inhabitants in the urban communities of Lagos, but with a computed rate of 3.1 per 1000 [57]. A prevalence rate of 5.3 per 1000 among the inhabitants of Igbo-Ora, a community with comprehensive health facilities, with the highest age-specific prevalence ratio occurring below the age of 20 years i.e. within 5 to 14 years age group. This prevalence rate is lower than what obtains in most rural African communities and similar to that of Western countries [58]. The lower prevalence rate is probably due to the improved health facilities in this community. In another community-based study, a prevalence rate of 6.2 per 1000 among the residents of a rural Community of Edo-speaking people in Nigeria. [59]. The age distribution in Nigerians appears similar to that described among the Caucasians [60]. Between 70% and 85% of patients with epilepsy (PWE) have onset of seizures below 30 years of age. It was noted that the onset in 68% of patients was in the first and second decades of life. This was confirmed in a study among children over 5 years of age with a prevalence of 82%. Among adult Nigerians, a study reported a mean age of 21 years with dominance of partial seizures (53.3%) [3]. Most African studies reported a slight male excess [7]. It is thought that, in most parts of Africa, males more readily come to the hospital for socioeconomic reasons and hence predominate in the hospital populations. This pattern holds true for Nigerians with epilepsy [8]. The male sex preponderance may also be due to occupational and social exposure to epileptogenic insults such as cranial trauma and alcohol. Epilepsy tends to be more common in the lower socio-economic groups [9]. There was an increase incidence of epilepsy among the poor blacks in United States of America [17]. Several studies reported in Africa also confirmed a higher prevalence of epilepsy among rural dwellers [8]. These epidemiological findings are of importance as they imply that, at least part of the burden of the incidence of epilepsy can be solved by preventive methods to improve social health as certain risk factors have been identified to increase the prevalence of epilepsy [13]. In a case-control study in which Nigerian epileptic patients were compared with age and sex–matched controls, febrile convulsions and head trauma were significant risk factors for epilepsy, while childhood immunization was significantly associated with decreased prevalence [18]. Other studies have confirmed the importance of birth asphyxia, intracranial infections, hereditary factors and head injuries as important risk factors [20]. Many of these factors are preventable or modifiable and the introduction of appropriate measures to achieve this could lead to a substantial decrease in the incidence of epilepsy in developing countries[24]

GLOBAL PREVALENCE OF EPILEPSY

In the North American studies, the age adjusted prevalence was 5.0 in a study conducted in New York and 7.1 per 1000 in Mississippi [30]. In Central and South America, the overall age-adjusted prevalence ranged from 3.7 per 1000 in Argentina to 22.2 per 1000 in Ecuador [31]. The South American study has the lowest age-adjusted prevalence of 3.7. In Europe, age-adjusted prevalence was low, 2.7 per 1000 and 3.3 per 1000, respectively in each study conducted in Italy, when compared to a prevalence of 7.0 per 1000 in the study conducted in the European region of Turkey [32].

In contrast to the majority of studies conducted in Asia, the age-adjusted prevalence of 10.2 per 1000 in Asian Turkey was higher than both the age-adjusted prevalence of 6.6 per 1000 and 9.8 per 1000 in the studies conducted in Asian Turkey and Pakistan [32]. This prevalence was much higher than the age-adjusted prevalence reported in studies conducted in India and China, where prevalence ranged between 2.2

and 4.4 per 1000.[7] Prevalence is higher in males than females [7].

Few studies have examined prevalence of epilepsy comparing race or ethnic group [7]. The largest racially diverse prevalence study found age-adjusted prevalence was higher for African-Americans (8.2 per 1000) as compared to Caucasians (5.4 per 1000) [15]. While the study suggests a higher prevalence of epilepsy among African-Americans, a serious limitation was failure to control for socioeconomic status [16].

SOCIAL AND ECONOMIC IMPACTS OF EPILEPSY

Epilepsy accounts for 0.6%, of the global burden of disease, a time-based measure that combines years of life lost due to premature mortality and time lived in less than full health [7]. Epilepsy has significant economic implications in terms of health care needs, premature death and lost work productivity [7]. An Indian study calculated that the cost per patient of epilepsy treatment was as high as 88.2% of the country's per capita Gross National Product (GNP), and epilepsy-related costs, which included medical costs, travel, and lost work time, exceeded $2.6 billion/year [7]. Although the social effects vary from country to country, the discrimination, effects on education, marriage and social stigma that surround epilepsy worldwide are often more difficult to overcome than the seizures themselves [5]. People living with epilepsy can be targets of prejudice. The stigma of the disorder can discourage people from seeking treatment for symptoms, so as to avoid becoming identified with the disorder. Challenges of epilepsy care in resource poor countries include magnitude of the epilepsy burden, widespread poverty, high rate of illiteracy and lack of awareness about epilepsy, negative public attitude to epilepsy, widely prevalent stigma, myths and misconceptions about epilepsy, inadequate and inefficient health-care facilities, inequality in availability and accessibility of resources and services in the health sector, social and political instability, leading to disorganization of health services and migration of populations, severe shortage of epilepsy specialists and infrastructural facilities, all of which are required for advanced epilepsy care and lack of reliable information about resources and services for epilepsy care [5]. People with epilepsy can experience reduced access to health and life insurance, a withholding of the opportunity to obtain a driving license, and barriers to enter particular occupations, among other limitations [7].

SIGNS AND SYMPTOMS OF EPILEPSY

The signs and symptoms of seizures vary and depend on where in the brain the disturbance first starts, and how far it spreads. Temporary symptoms occur, such as loss of awareness or consciousness, and disturbances of movement, sensation (including vision, hearing and taste), mood, or other cognitive functions [17]. People with seizures tend to have more physical problems (such as fractures and bruising from injuries related to seizures), as well as higher rates of psychological conditions, including anxiety and depression [16]. Similarly, the risk of premature death in people with epilepsy is up to 3 times higher than the general population, with the highest rates found in low and middle-income countries and rural versus urban areas [16]. A great proportion of the causes of death related to epilepsy in low- and middle-income countries are potentially preventable, such as falls, drowning, burns and prolonged seizures [16].

INVESTIGATIONS

In evaluating patients with epilepsy, the aim is to determine what type of seizures they are having and their cause. The investigations are electroencephalogram; Blood tests (complete blood count and chemistry panel e.g. serum electrolytes, urea and creatinine, Serum calcium); Brain imaging (Brain Computed Tomography (CT) or Brain Magnetic Resonance Imaging (MRI)) though the imaging of choice is Brain MRI; Positron emission tomography (PET) scan and Spinal Tap.

MANAGEMENT OF EPILEPSY

Epilepsy can be treated with a daily medication that costs as much as US$ 5 (1,800 Naira) per month [17]. Recent studies in both low- and middle-income countries have shown that up to 70% of children and adults with epilepsy can be successfully treated (i.e. their seizures completely controlled) with anti-epileptic drugs (AEDs) [17]. After 2 to 5 years of successful treatment and being seizure-free, drugs can be withdrawn in about 70% of children and 60% of adults without subsequent relapse [17]. In the treatment of patients with epilepsy, low and middle income countries, about three fourths of people with epilepsy may not receive the treatment they need [17]. This is called the "treatment gap". In many low and middle income countries, there is low availability of AEDs. A recent study found the average availability of generic antiepileptic medicines in the public sector of low- and middle-income countries to be less than 50% [17]. This may act as a barrier to accessing treatment. It is possible to diagnose and treat most people with epilepsy at the primary health- care level without the use of sophisticated equipment.

Medications are the mainstays in controlling epileptic seizures. There have been some studies of alternative treatments for epilepsy, including biofeedback, melatonin, and large doses of vitamins [7,18]. Vagus nerve stimulation is another form of treatment whereby a doctor implants a pacemaker-like device in the body to stimulate the left vagus nerve. Surgical procedures are another way epilepsy can be treated, they include; multiple subpial transection; temporal lobe resection; lesionectomy; functional hemispherectomy, corpus callostomy, extratemporal cortical resection. Use of ketogenic diet (a diet very high in fat and low in carbohydrates) is one of the oldest treatments for epilepsy [19]. In all, majority of epileptic seizures are controlled through drug therapy [7,8,18].

DRUG TREATMENT (ANTI-EPILEPTIC DRUGS)

Drugs used to treat seizures are called antiepileptic drugs (AEDs). There are two types of seizure drugs: narrow-spectrum AEDs and broad-spectrum AEDs.

NARROW-SPECTRUM AEDS

Narrow-spectrum AEDs are designed for specific types of seizure [8,18]. The narrow-spectrum AEDs are as follows: Carbamazepine, Clobazam, Diazepam, Divalproex,Eslicarbazepine, Ethosuximide, Gabapentin, Lacosamide, Methsuximide, Oxcarbazeopine, Perampanel, Phenobarbital, Phenytoin, Pregabalin, Rufinamide, Tigabadine and Vigabatrin.

BROAD-SPECTRUM AEDs

In a case of more than one type of seizure, a broad-spectrum AED may be the best choice of treatment [8]. These drugs are designed to prevent seizures in more than one part of the brain while narrow-spectrum AEDs work in one specific part of the brain [8]. Broad-spectrum AEDs include Clonazepam, Clorazepate, Ezogabine, Felbamate, Lamotrigine, Levetiracetam, Lorazepam, Primidone, Topiramate, Valporic acid and Zonisamide [8].

Table 1:The spectrum of efficacy of different types of AEDs

FOCAL SEIZURES	Carbamazepine, Levetiracetam, Lamotrigine, Topiramate, Tiagabine, Pregabalin, Perampanel, Valporate, Felbamate, Gabapentin, Ezogabine, Eslicarbazepine, Phenobarbital, Phenytoin, Oxcarbazepine, Vigabatrin, Zonasamide, Lacosamide and Rufinamide. They are proven class 1 trials. Primidone and Clobazam can be suggested but not proven in class1 trials. Ethosuximide is not effective.
GENERALISED TONIC CLONIC SEIZURES	Proven class 1 trials include Lamotrigine, Topiramate, Levetiracetam and Perampanel. Suggested but not proven in class1 trials include Phenobarbital, Rufinamide, Phenytoin, Carbamazepine, Primidone, valproate, Clobazam, Felbamate and Zonasamide. Not effective include Gabapentin, Pregabalin, Tiagabine and Ethosuximide.
GENERALISED ABSENCE SEIZURES	Class 1 trial drugs are valproate and Ethosuximide. Suggested but not class 1 trial drugs are Clobazam, Lamotrigin, Levetiracetam and Zonasamide.
GENERALISED MYOCLONIC SEIZURES	Class 1 trial drug is levetiracetam. Class 4 evidence are Phenobarbital and Primidone. Suggested include valproate, Clobazam and Zonasamide

PROGNOSIS

Generalized seizures are more readily controlled than partial seizures [21]. Childhood onset epilepsy (particularly classical absence seizures) carries the best prognosis for successful drug withdrawal [15]. The presence of a structural lesion makes complete control of epilepsy less likely [16]. The pattern of outcome of epilepsy after 20 years is as follows;

- 50% seizure-free, without drugs, for last 5 years.
- 20% seizure-free, continue to take medication, for last 5 years.
- 30% seizures continue in spite of adequate dose of AEDs.
- Refractory epilepsy which is defined as when seizure control is not achieved with the first two appropriate drugs that are well tolerated.

WITHDRAWAL OF AEDs

After complete control of seizures for 2-4 years, withdrawal of anti-epileptic drugs may be considered [4]. In case of special professional groups (for example a car driver, machine operator), withdrawal of the AED is after keen follow-up. AED should be gradually tapered during the stopping of medications. Slow reduction by increments over at least 4-6 months [4]. If the patient is taking two AEDs, one drug should be slowly withdrawn before the second is tapered [4].

PREVENTION OF EPILEPSY

Idiopathic epilepsy is not preventable [1,2]. However, preventive measures can be applied to the known causes of secondary epilepsy. These measures include;

- Preventing head injury which is the most effective way to prevent post-traumatic epilepsy.
- Adequate perinatal care can reduce new cases of epilepsy caused by birth injury.
- Central nervous system infections are common causes of epilepsy in tropical areas, where many low- and middle-income countries are concentrated thus there is need for their prevention and proper treatment.
- Elimination of parasites in these environments and education on how to avoid infections can be effective ways to reduce epilepsy worldwide, for example those cases due to neurocysticercosis.

COGNITION

Cognition is the ability to assimilate and process information received from different sources (perception, experience, beliefs) and convert them

into knowledge. Cognition includes different cognitive processes, like learning, attention, memory, language, reasoning, decision making, which form part of our intellectual development and experience. Different disciplines have studied cognition, like neurology, psychology, anthropology, philosophy, and even information sciences and emotions. Cognitive processes are the procedures we use to incorporate new knowledge and make decisions based on said knowledge. Different cognitive functions play a role in these processes: perception, attention, memory and reasoning.

PATHOPHYSIOLOGY OF COGNITIVE IMPAIRMENT IN EPILEPSY

The aetiology of seizure has a role to play in cognition [7]. Prolonged and recurrent seizures can cause or exacerbate cognitive impairment [6,7,8,9]. Alterations in signaling pathways and neuronal network function play major role in both the pathophysiology of epilepsy (the imbalance in mechanism that regulate between excitatory and inhibitory neuronal activities) and the epilepsy comorbidities [23,24].The pathophysiology depends on the risk factors affecting cognition which include frequency of seizures, duration and severity of seizures, the type of seizures, age of epilepsy onset, structural cerebral lesions responsible for the development of epilepsy, sequelae of epileptic surgery, side effects of drugs and psychosocial factors [9,14].

Recurrent seizures affect cognition acutely [7]. Frequent seizures cause cumulative degradation in spatial performance [7]. It results in impairment in long term potentiation, the precision and frequency and frequency of theta oscillation that represent the orderly communication of networks, all factors which could negatively affect cognition [6]. It can also lead to persistent decrease in GABA current in hippocampus and neocortex, enhanced excitation in the neocortex, impairment in spike frequency adaptation, marked reductions in after hyperpolarising potentials following spikes train, alteration in theta power and precision in place of firing precision and stability [6].

EPILEPSY AND COGNITION

Cognitive decline has long been recognized as a sequel of intractable epilepsy [6]. A number of factors have been identified as having a role, including underlying pathology, seizures, and medication. Of the main factors identified, the role of seizures has been less well studied, and the available evidence does not indicate as strong a relation as might be anticipated from clinical experience and animal studies [6]. Research involving animal models of epilepsy has demonstrated that status epilepticus and frequent, recurrent, chemically and electrically induced seizures can result in cognitive impairment [6]. Cross-sectional studies of humans have provided some evidence of a relation between seizure frequency and cognitive impairment [23]. Longer duration of epilepsy has been reported to be associated with greater cognitive impairments [25]. The negative impact of duration may be in part due to the cumulative impact of seizures, but also to other factors including antiepileptic drug (AED) treatment and pathologic interictal brain activity [25]. Two studies have estimated cognitive decline on the basis of language abilities [14]. One found a relation between cognitive decline and seizure severity but not frequency, and the other reported that duration of epilepsy was the best predictor of cognitive decline, and other epilepsy-related variables did not make any additional contribution to the variance [14].

[26], reviewed nine longitudinal studies that measured intellectual functioning in children followed up for a maximum of 4 years. Several of other studies reported intellectual decline, and [26] concluded that poorly controlled seizures were likely to have some causal role. Rodin reported intellectual decline in adults with poorly controlled seizures in contrast to improved intellectual functioning in patients who had experienced periods of remission ≥2 years in the inter-test interval [27]. Similarly, [28], reported intellectual gains in association with improved seizure control [28] Other investigators reported stable cognitive functioning in

individuals with good seizure control and, conversely, a poorer cognitive outcome in patients with continuing seizures [28]. No cognitive change, however, has been noted in some studies in association with continuing seizures [28].

COMPUTERIZED COGNITIVE ASSESSEMENT TESTS

Clinical neuropsychological assessment methods utilised in the study of cognitive functions have undergone considerable evolution from the early days when estimates were based solely on clinical impression to much broader and more sophiscated techniques which is actually more scientific and specific [11]. Computerized neuropsychological tests usually have a high objectivity in terms of administration and scoring [13]. In contrast to paper-pencil testing, computer tests allow for the exact assessment of reaction times in milliseconds [11]. Although the application does not necessarily require neuropsychological expertise, computerized testing without neuropsychological supervision bears the risk of false interpretations [13].

A major advantage of computerized testing, especially for the field of epilepsy, is the possibility of time-locked co-registration of cognitive processes and physiological measures [11]. This means the impact of inter-ictal epileptiform discharges on cognitive performance can be analyzed [11]. Apart from concomitant EEG-analyses, computerized tests can also be applied during functional brain imaging studies (e.g. fMRI) [11]. Computerized neuropsychological tests may also have some disadvantages. Self-administrable computerized tests dramatically reduce the interaction between examiner and patient. Another disadvantage can be seen in interface problems, for example, behavioral responses are reduced to reactions via mouse, keyboard or joystick. The exact position of the index finger (the distance between finger and key) may be important for the measurements of reaction times in milliseconds. The increasing availability of more intuitive touchscreens may attenuate such reservations. Future and advanced techniques of video-monitoring, language recognition or movement registration may expand the variety of behavioral expressions. Some computerized neuropsychological tests in the field of epilepsy include [5].

- FEPSY " The Iron Psyche"
- California Computerized Assessment Package (CALCAP)
- Cambridge Neuropsychological Test Automated Battery (CANTAB)
- Computerized Cognitive Testing in Epilepsy (CCTE)
- Cognitive Drug Research (CDR) computerized assessment system
- Cognitive Neurophysiological Test (CNT)
- Computerized Neuropsychological Test Battery (CNTB)
- NeuroCog FX
- Test of attentional performance (TAP)

FePsy 'The Iron Psyche'

The new version of FePsy comprises a battery of 16 computerized tests which are auditory reaction time, visual reaction time, binary choice reaction time, tapping task, computerized visual searching task, verbal and visual recognition tasks, vigilance task, rhythm task, card sorting task, visual half field tasks, Corsi block tapping, recognition simultaneously and serially testing, classification tasks, Binnie's block test, continuous EEG, image tasks, as well as a memory and a cognitive complaints questionnaire) for cognitive neuropsychological functions and is built around a powerful relational database system which stores all results. These results can easily be converted into statistical or other database programs. FePsy includes a subset of tests for the measurement of side effects of drugs (Epilepsy, Cancer, HIV) and is also used in other fields (Parkinson, Schizophrenia, Diabetes), covering arousal, short-term memory, mental speed, vigilance, naming as well as some questionnaires. A factor analysis in 747 patients with epilepsy revealed six factors reflecting (1) working memory/memory/attention, (2) simple reaction time, (3) motor performance, (4) problem solving, (5) choice reaction time, (6) impulsivity.[44] It runs on every modern personal computer.[44] Use of a touchscreen is an option. FePsy is available in almost all

European languages, 21 in total. FePsy easily connects to the EEG to analyze simultaneous EEG signals and psychological performance.

The computerized tests to be incorporated in standard neuropsychological assessment remains a matter of choice. It is important that tests to be used must have been validated and standardized. It is important to emphasize that, in most diagnostic situations, exclusive computerized testing in epilepsy cannot yet substitute a thorough neuropsychological examination of patients with epilepsy, especially not in surgical settings. Irrespective of the testing procedure, validity (clinical and ecological) must be the major selection criterion for neuropsychological instruments [11]. Thus, published evidence is essential to prove the suitability of tests with regard to specific diagnostic questions. Only this will ensure an evidence-based future for neuropsychologicaltesting.

MONTREAL COGNITIVE ASSESSMENT (MOCA)

The Montreal Cognitive Assessment (MOCA) is a cognitive screening tool that was designed as a rapid screening instrument for mild cognitive impairment (MCI). It is a simple 10 minutes paper and pencil test that assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuo-constructional skills, conceptual thinking, calculations and orientation. Its validity has been established to detect mild cognitive impairment in patients with Alzheimer's disease and other pathologies in cognitively impaired subjects who scored in the normal range on the mini mental state examination (MMSE) [37]. MOCA's sensitivity and specificity to detect subjects with MCI due to Alzheimer's disease and distinguish them from healthy controls are excellent [38]. MOCA is also sensitive to detect cognitive impairment in Epilepsy, Cerebrovascular disease, Parkinson's disease, Huntington's disease, brain tumors, SLE, substance use disorders, idiopathic rapid eye movement sleep behavior disorder, obstructive sleep apnea, risk of falling, rehabilitation outcome, chronic obstructive pulmonary disease and HIV infection [38]. There are several features in MOCA's design that likely explain its superior sensitivity for detecting MCI. MOCA's memory testing involves more words, fewer learning trials, and a longer delay before recall than the MMSE. Executive functions, higher level language abilities, and complex visuo-spatial processing can also be mildly impaired in MCI participants of various aetiologies and are assessed by the MOCA with more numerous and demanding tasks than the MMSE [37,39]. MOCA was developed in a memory clinic setting and normed in a highly educated population. The total possible score is 30 points, a score of 26 or above is considered normal.

CONCLUSION

Idiopathic epilepsy is not preventable. However, preventive measures can be applied to the known causes of secondary epilepsy.

REFERENCES

1. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014;55:475–82.
2. Fisher RS, Cross JH, French JA, Higurashi N, Peltola J, Roulet E, et al. Operational classification of seizure types by the International League Against Epilepsy : Position Paper of the ILAE Commission for Classification and Terminology. 2017;522–30.
3. Nazmetdinova DM, Basamygin A V, Kalinin V V. [Memory and intellectual disorders in patients with epilepsy: an analysis of the relationship between clinical characteristics and brain asymmetry]. Zhurnal Nevrol i psikhiatrii Im SS Korsakova. 2010;110:82–7.
4. Beretta S, Carone D, Zanchi C, Bianchi E, Pirovano M, Trentini C, et al. Long-term applicability of the new ILAE definition of epilepsy. Results from the PRO-LONG study. Epilepsia. 2017;58:1518–23.
5. Ogunrin O, Adamolekun B,

Ogunniyi AO, Aldenkamp AP. Cognitive Function in Nigerians with Newly Diagnosed Epilepsy. Can J Neurol Sci. 2017;148–51.
6. Hermann B, Seidenberg M. Epilepsy and cognition. Epilepsy Curr. 2007;7:1–6.
7. Gulati S, Yoganathan S, Chakrabarty B. Epilepsy, cognition and behavior. Indian J Pediatr. 2014;81:1056–62.
8. Hamed SA. The aspects and mechanisms of cognitive alterations in epilepsy: the role of antiepileptic medications. CNS Neurosci Ther. 2009;15:134–56.
9. Japaridze N, Menzel E, von Ondarza G, Steinmann E, Stephani U. Risk factors of cognitive outcome in patients with atypical benign partial epilepsy/pseudo-Lennox syndrome (ABPE/PLS) and continues spike and wave during sleep (CSWS). Eur J Paediatr Neurol. 2014;18:368–75.
10. Realmuto S, Zummo L, Cerami C, Agro L, Dodich A, Canessa N, et al. Social cognition dysfunctions in patients with epilepsy: Evidence from patients with temporal lobe and idiopathic generalized epilepsies. Epilepsy Behav. 2015;47:98–103.
11. Baxendale S. Neuropsychological assessment in epilepsy. Vol. 18, Practical neurology. England; 2018. p. 43–8.
12. Witt J-A, Helmstaedter C. Cognition in epilepsy: current clinical issues of interest. Curr Opin Neurol. 2017;30:174–9.
13. Arinzechi EO, Ogunrin OA, Nwosu CM, Nwani PO, Enwereji KO, Asumogha LA, et al. A community-based case-control study of prevalence and pattern of cognitive impairments in patients with epilepsy residing in South-Eastern Nigeria. J Neurosci Rural Pract. 2016;7:405–11.
14. Meador KJ. Cognitive outcomes and predictive factors in epilepsy. Neurology. 2002;58:S21-6.
15. Braakman HMH, Vaessen MJ, Hofman PAM, Debeij-Van Hall MHJA, Backes WH, Vles JSH, et al. Cognitive and behavioral complications of frontal lobe epilepsy in children: A review of the literature. Epilepsia. 2011;52:849–56.
16. Greener M. Beyond seizures : understanding. 2013;31–2.
17. Hirsch E, Schmitz B, Carreno M. Epilepsy, antiepileptic drugs (AEDs) and cognition. Acta Neurol Scand. 2003;108:23–32.
18. Helmstaedter C, Witt J-A. The longer-term cognitive effects of adjunctive antiepileptic treatment with lacosamide in comparison with lamotrigine and topiramate in a naturalistic outpatient setting. Epilepsy Behav. 2013;26:182–7.
19. Hallböök T, Ji S, Maudsley S, Martin B. The effects of the ketogenic diet on behavior and cognition. Epilepsy Res. 2012;100:304–9.
20. Karnam HB, Zhou J-L, Huang L-T, Zhao Q, Shatskikh T, Holmes GL. Early life seizures cause long-standing impairment of the hippocampal map. Exp Neurol. 2009;217:378–87.
21. Mula M. Emerging drugs for focal epilepsy. Expert Opin Emerg Drugs. 2018;23:243–9.
22. Kwan P, Brodie MJ. Neuropsychological effects of epilepsy and antiepileptic drugs. Lancet. 2001;357:216–22.
23. Miller LA, Galioto R, Tremont G, Davis J, Bryant K, Roth J, et al. Cognitive impairment in older adults with epilepsy: Characterization and risk factor analysis. Epilepsy Behav. 2016;56:113–7.
24. Helmstaedter C. Cognitive outcome of status epilepticus in adults. Epilepsia. 2007;48:85–90.
25. Elger CE, Helmstaedter C, Kurthen M. Chronic epilepsy and cognition. Lancet Neurol. 2004;3:663–72.
26. Dodrill CB. Progressive cognitive decline in adolescents and adults with epilepsy. Prog Brain Res. 2002;135:399–407.
27. Rodin G, Ahles TA. Accumulating evidence for the effect of chemotherapy on cognition. J Clin Oncol. 2012;10:3568–9.
28. Seidenberg M, Pulsipher DT, Hermann B. Cognitive progression in epilepsy. Neuropsychol Rev.

2007;17:445–54.
29. Loring DW, Williamson DJ, Meador KJ, Wiegand F, Hulihan J. Topiramate dose effects on cognition: a randomized double-blind study. Neurology. 2011;76:131–7.
30. Park SP, Kwon SH. Cognitive effects of antiepileptic drugs. J Clin Neurol. 2008;4:99–106.
31. Nicolai J, Kasteleijn-Nolst Trenite D. Interictal discharges and cognition. Epilepsy Behav. 2011;22:134–6.
32. Piazzini A, Turner K, Vignoli A, Canger R, Canevini MP. Frontal cognitive dysfunction in juvenile myoclonic epilepsy. Epilepsia. 2008;49:657–62.
33. Witt J-A, Werhahn KJ, Kramer G, Ruckes C, Trinka E, Helmstaedter C. Cognitive-behavioral screening in elderly patients with new-onset epilepsy before treatment. Acta Neurol Scand. 2014;130:172–7.
34. Subota A, Pham T, Jette N, Sauro K, Lorenzetti D, Holroyd-Leduc J. The association between dementia and epilepsy: A systematic review and meta-analysis. Epilepsia. 2017;58:962–72.
35. Power KN, Gramstad A, Gilhus NE, Hufthammer KO, Engelsen BA. Cognitive dysfunction after generalized tonic-clonic status epilepticus in adults. Acta Neurol Scand. 2018;137:417–24.
36. Ogunrin, Olubunmi A AB. Cognitive neuroassessment in Nigeria Africans-Predictive validity of a computerized testing. Ann Biomed Sci. 2007;6:26–45.
37. Trzepacz PT, Hochstetler H, Wang S, Walker B, Saykin AJ. Relationship between the Montreal Cognitive Assessment and Mini-mental State Examination for assessment of mild cognitive impairment in older adults. BMC Geriatr. 2015;15:107.
38. Beath N, Asmal L, van den Heuvel L, Seedat S. Validation of the Montreal cognitive assessment against the RBANS in a healthy South African cohort. South African J Psychiatry. 2018;24:9685.
39. Phabphal K, Kanjanasatien J. Montreal Cognitive Assessment in cryptogenic epilepsy patients with normal Mini-Mental State Examination scores. Epileptic Disord. 2011;13:375–81.
40. Kish L. Survey sampling. John Wiley sons, Inc. 1965;78–94.
41. Sunmonu T. A, Komolafe M.A, Ogunrin O. A OA. Cognitive assessment in patients with epilepsy using the community screening interview for Dementia. Epilepsy Behav. 2009;14:535–9.
42. D MM. Prevalence of cognitive adverse outcomes in epileptic outpatients using MMSE. J Neurol Stroke. 2016;4:1–11.
43. M S. Epilepsy in children:Prevalence, disability and handicap. Epilepsia. 1992;33:444–9.
44. Aikia¨, M, Salmenpera T, Partanem K KR. Verbal memory in newly diagnosed patients and patients with chronic left temporal lobe epilepsy. Epilepsy Behav. 2001;2:20–7.
45. Kalviainen R, Aikia M HEL et al. Memory and attention in newly diagnosed epileptic seizures disorder. Seizure. 1992;1:255–62.
46. Witt, J-A, Werhahn K. J, Kramer G, Ruckes C, Trinka E HC. Cognitive behavioural screening in elderly patients with new-onset epilepsy before treatment. Acta Neurol Scand. 2014;130:48–56.
47. Hermann B, Meador KJ, Gaillard WD, Cramer JA. Cognition across the lifespan: Antiepileptic drugs, epilepsy, or both? Epilepsy Behav. 2010;17:1–5.
48. Witt J-A, Helmstaedter C. Cognition in the early stages of adult epilepsy. Seizure. 2015;26:65–8.
49. Witt, Juri-Alexander HC. Should cognition be screened in new onset epilepsies? J Neurol Neurosurg Psychiatry. 2012;259:1727–31.
50. Aldenkamp, Albert P, Alpherts W. C DMJ et al. Neuropsychological aspects of learning disabilities in epilepsy. Epilepsia. 1990;31:9–20.
51. Williams J, Philips T GM et al. Factors associated with academic achievement in children with

controlled epilepsy. Epilepsy Behav. 2001;2:217–23.
52. McNeils A. M, Johnson C. S, Huberty T. J et al. Factors associated with academic schievement in children with recent seizures. Seizure. 2005;14:331–9.
53. Mitchel W G, Zhou Y CJM et al. Reaction time, attention and impulsivity in epilepsy. Paediatr Neurol. 1992;8:19–24.
54. L BL. The impact of childhood epilepsy on neurocognitive and behavioral performance: A prospective study. Epilepsia. 2000;41:426–31.
55. Mc Carthy A. M, Richmond E YD. Memory, attention and school problems in children with seizure disorders. Dev Neuropsychol. 1995;11:71–86.
56. Mula, M TMR. Antiepileptic drug induced cognitive adverse effects potential mechanism and contributing factors. CNS Drugs. 2009;23:121–37.
57. Mula M. Recent and future epileptic drugs and their impact on cognition: what can we expect? Expert Rev Neurotheurapeutics. 2012;12:667–71.
58. Perucca, P MM. Antiepileptic drug effects on mood and behaviour molecular targets. Epilepsy Behav. 2013;26:440–9.
59. Dodrill CB. Neuropsychological effects of seizures. Epilepsy Behav. 2004;1:S21-24.
60. Epilepsy fact sheet [Internet]. World Health Organisation. 2017. Available from: https://www.who.int/news-room/fact-sheets/detail/epilepsy