

## Management of epilepsy in elderly

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The prevalence of seizures and epilepsy in the elderly is generally underestimated. Epileptic seizures are not a rare occurrence in the elderly and their prevalence increases with age. The clinical manifestations of seizures, the aetiology, the treatment and the psychosocial impact of the epilepsy diagnosis may differ in the elderly. Differential diagnosis with episodes of unconsciousness and/or fall or other non-epileptic manifestations is often difficult. The presence of comorbidities, the polypharmatherapy and the age-related pharmacokinetic changes can represent a problem for the treatment of epilepsy in the elderly, with a higher risk of adverse effects and potentially inappropriate drug interactions. Epileptic seizures in the elderly can have semiological characteristics similar to those of other age groups. On the other hand, the richness of the electroclinical syndromes of childhood and adolescence is not found in the elderly, and, in particular, idiopathic generalized epilepsies are rarely expressed at this age. Symptomatic seizures related to acute structural injury or metabolic causes are particularly frequent. Therapy management of the elderly with an epileptic seizure should concern not only neurologists, but also general practitioners, geriatricians, and cardiologists, therefore involving a wide range of clinical specialties. This review aims to summarize the management of epilepsy in the elderly, reporting also differences in epidemiology, electroclinical features, aetiology and diagnostic procedures.

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## INTRODUCTION

The prevalence of seizures and epilepsy in the elderly is generally underestimated. The reasons can be found in the idea of a rather rare occurrence of the condition; but also in the general impression that experiencing an epileptic seizure in the elderly represents a less important problem than in a young person; and that diagnostic and therapeutic solutions can be directly achieved from studies performed in a younger population, rather than from trials specifically designed for old age. Actually the impression that epilepsy in the elderly is an irrelevant topic is very far from the truth, representing instead a real prejudice.

Epileptic seizures are not a rare occurrence in the elderly and their prevalence increases with age. The clinical manifestations of seizures, the

aetiology, the treatment and the psychosocial impact of the epilepsy diagnosis may differ in the elderly. Differential diagnosis with episodes of unconsciousness and/or fall or other non-epileptic manifestations is often difficult. The presence of comorbidities, the polypharmatherapy and the age-related pharmacokinetic changes can represent a problem for the treatment of epilepsy in the elderly, with a higher risk of adverse effects and potentially inappropriate drug interactions <sup>1</sup>. Elderlies are more vulnerable to the sequelae of seizures due to physical and psychological trauma, with loss of confidence in autonomy and reduced degree of independence. The concurrence of osteoporosis multiplies the risk of fractures. Fears of seizures and falls can confine an elder at home, or in armchair. Due to seizures, or fear of seizures, the elderly are often excluded and marginalized by the activities. The driving license revocation can greatly limit autonomy and quality of life. Finally, older people have mortality rates 2 or 3 times higher than the general population <sup>2,3</sup>. For all these reasons, the management of the elderly with epilepsy should concerns not only to neurologists, but also general practitioners, geriatricians, and cardiologists, therefore involving a wide range of clinical specialties. With the worldwide-distributed increase of the elderly population, the problem has also assumed a considerable economic importance, with a growing weight for health care expenditure.

## EPIDEMIOLOGY

From the Hauser' study on the Rochester population <sup>4</sup>, it is possible to evaluate how the incidence of epilepsy, substantially stable between the second and fifth decades of life with 30-40 cases/100,000 persons/year, starts to grow up from the age of 60's, reaching an incidence of around 150 cases/100,000 persons/year in the 80 years old subjects. As expected, the main contribution to increasing epilepsy incidence is given by focal seizures (over 100 cases/ 100,000 persons/ year at 80 years), in relation to the typical aetiology from injury rather than the generalized attacks (around 40 cases/100,000 persons/ year at the same age). Hersdorffer et al. <sup>5</sup> investigated the cumulative incidence and probability of a person to develop epilepsy over lifetime (lifetime risk) starting from the current age. The authors calculated that one person out of 26 (1/21 males and 1/28 females) will develop epilepsy during his/her lifetime. This parameter is useful both for clinical and health planning purposes because it allows to predict the weight of the disease in the community. However, the rapid growth in the world of the elderly population, the different prevalence of several diseases expressing with

seizures in different countries, the difficulty in collecting data, and the various methodologies used, make it difficult to accurately estimate the incidence of Epilepsy in the elderly, possibly explaining discrete dissimilarities found in other epidemiological studies <sup>6</sup>. It is however evident that epileptic seizures and epilepsy represent a frequent problem of considerable importance in this age of life <sup>7</sup>. Therefore, rather than proceeding on the difficult field of epidemiology, it is more useful to recall some definitions that will occur below (Tab. I).

## ELECTROCLINICAL FEATURES OF SEIZURES

Epileptic seizures in elderly can have semiological characteristics similar to those in other age groups. On the other hand, the richness of the electroclinical syndromes of childhood and adolescence is not found in the elderly <sup>8</sup>, and in particular idiopathic generalized epilepsies are very rarely expressed at this age <sup>9</sup>. In relation to age-specific aetiologies, the contribution of different seizures types (clear prevalence of partial, simple or complex seizures, with or without secondary generalization) and of epileptic syndromes (greater prevalence of symptomatic epilepsies than idiopathic ones), and acute symptomatic seizures related to structural injuries or metabolic causes are particularly frequent. It is also necessary to point out some milestones:

- the post-ictal status can be particularly prolonged, and a post-ictal hemiparesis (Todd's paralysis) is frequently found, sometimes raising the issue with a differential diagnosis of stroke;
- some types of seizures are peculiar of the elderly, such as confusional states with periodical lateralized epileptiform discharges (PLEDs) and transient epileptic amnesia (TEA);
- status epilepticus is particularly frequent in the elderly, often marking the onset of epilepsy or in the context of acute symptomatic seizures, and is burdened by frequent mortality <sup>3,10</sup>. Myoclonic seizures following cardiac arrest and cardio-respiratory resuscitation are characterized by poor prognosis, with over 90% of death or persistent vegetative status <sup>2</sup>. Non-convulsive status epilepticus must be considered in the differential diagnosis of confusional disorders in elderly <sup>11</sup>;
- the contribution of intercritical EEG in diagnosis is generally less relevant than in the Epilepsies of childhood-adolescence-youth. Ictal recordings, on the other hand, are crucial, allowing the recognition of confusional disorders associated with PLEDs <sup>12</sup> and non-convulsive status epilepticus that would otherwise be difficult to diagnose.

## AETIOLOGY OF SEIZURES AND EPILEPSY IN ELDERLY

The high incidence and prevalence of seizures in the elderly are related to the high frequency of diseases

**Table I.** Operative definitions.

Terms	Definition	Note
Epileptic seizure	Transient occurrence of signs and/or symptoms due to an abnormal and excessively synchronized discharge of a neuronal population	It is not synonymous of Epilepsy!
Epilepsy	Condition characterized by a persistent tendency to generate epileptic seizures	Epidemiological studies are based on the presence of at least 2 chronologically distinct unprovoked seizures
Epilepsy in the elderly	Epilepsy that occurs after the age of 65. <i>Chronological age is also of relative importance; the probability of developing seizures is rather correlated with biological age</i>	To be distinguished from a pre-existing epilepsy for many years in an elderly patient, "aged" epilepsy
Acute symptomatic seizures	Seizures chronologically correlated with an event that alters the metabolic or structural homeostasis of neuronal function	An acute symptomatic seizure is not in itself a predictor of the onset of epilepsy
Immediate or very early seizures	Attacks that occur within seconds or minutes of acute brain damage	
Early seizures	Seizures occurring within the first week of the acute event	Some authors extend the period up to 1 month from the acute event
Late seizures	Seizures that appear more than a week after an acute event	
Remote symptomatic epilepsy	Epilepsy residual to a previous brain damage	
Status epilepticus	Condition characterized by prolonged or repeated seizures for at least 30 minutes	
Syncope	Abrupt, transient and complete loss of consciousness, associated with inability to maintain postural tone, with rapid and spontaneous recovery. The responsible pathophysiological mechanism is cerebral hypoperfusion	

representing risk factors for epilepsy (cerebrovascular, degenerative diseases, cancers, traumas; metabolic disorders etc). Furthermore, case-control studies suggest that aging itself may have an epileptogenic effect<sup>13</sup>. In the Lühdorf et al.<sup>14</sup> study, the most frequent cause was represented by stroke (32%) followed by cancers (14%); a significant portion was attributable to consumption of alcohol or drugs. Finally, about a quarter of cases remains of unknown reason, and, despite the improvement in neuroradiological investigations, the percentage of events without evidence of Central Nervous System (CNS) structural lesions remains high. However, even considering that it is the most frequent source of CNS damage, stroke very frequently causes seizures and epilepsy in the elderly. Seizures can occur at the time of stroke, even be an early clinical manifestation of cerebrovascular disease (acute symptomatic seizures), or they can appear later. Risk of epilepsy increases up to 20 times in the first year after a stroke. Epilepsy is most likely to occur if the stroke involves the cortex, if it is extensive or multiple, hemorrhagic and accompanied by acute symptomatic seizures<sup>3,15</sup>. The association of epileptic seizures with cerebrovascular disease appears to be bidirectional, so that the appearance of an epilepsy in elderly is accompanied by an approximately three-fold increase in risk of a subsequent stroke<sup>16</sup>. Therefore the appearance

of seizures in an elderly requires a careful search for a possible underlying vasculopathy, the identification of possible risk factors and a preventive therapy.

Both epilepsy and hypertension are frequent, chronic diseases that can coexist in the same individual. Hypertension may be a cause of seizures and epilepsy through direct or indirect mechanisms. Large-artery stroke, small vessel disease and posterior reversible leukoencephalopathy syndrome are hypertension-related brain lesions able to determine epilepsy by indirect mechanisms. However, hypertension is a predictor of late-onset epilepsy also independently from vascular damage, and renin-angiotensin system might play a central role in the direct interaction between hypertension and epilepsy. In addition, posterior reversible encephalopathy syndrome (PRES) is an acute condition, often caused by hypertensive crisis, associated with the occurrence of acute symptomatic seizures<sup>17</sup>.

Epileptic seizures are a frequent occurrence in the history of a patient with dementia, in particular with a risk up to 10 times greater in Alzheimer disease (AD) patients<sup>3</sup>. Seizures can appear at every stage of the disease, but especially in the advanced phases. AD and other neurodegenerative diseases constitute the cause of 10-20% of all epilepsies of the elderly. Duration, severity and age of dementia onset are risk

factors for the development of epilepsy, while there are insufficient data regarding the possibility of developing dementia in patients with epilepsy<sup>18</sup>. Some authors suggest that subclinical epileptiform activity in patients with Alzheimer's disease, detected by extended neurophysiological monitoring, can also lead to accelerated cognitive decline<sup>19</sup>.

Head trauma is common in elderly, and its consequences are often severe. Epilepsy lasting to head injury is a frequent occurrence, particularly if parenchyma contusion, subdural hematoma, skull fracture and prolonged coma occurred<sup>3</sup>.

Between 10 and 30% of seizures in the elderly are related to both primary and secondary CNS cancers<sup>3</sup>. Seizures are often the revealing symptom of the cancer. Generally, epilepsy associated with a brain cancer is more frequent in primary and slow-growing brain tumors.

Acute metabolic disorders and infections can cause acute symptomatic seizures. Up to 19% of patients with non-ketotic hyperglycaemia develop somatomotor focal seizures, often reflexes and sometimes an *epilepsia partialis continua*, often resistant to the classic antiepileptic drugs, with phenytoin that can worsen the symptoms by inhibiting the release of insulin<sup>2</sup>. Obstructive sleep apnoea syndrome can lower the seizure threshold in elderly patients with epilepsy<sup>20</sup>.

Many drugs can be responsible for seizures. Different classes of drugs can induce acute symptomatic epileptic seizures (Tab. II), often as a consequence

of an increased exposure caused by a reduced clearance, a frequent occurrence in elderly<sup>21</sup>, although the correlation between drug intake and attack onset is not explained in all cases from the mechanism of action, and the causal relationship is not always demonstrable.

#### DIAGNOSTIC PROCEDURE AND DIFFERENTIAL DIAGNOSIS

Diagnosis of epilepsy in the elderly requires special caution. At this age, in fact, numerous other disturbances of other nature are very frequent, in particular syncopal episodes<sup>22</sup>. The risk of diagnostic errors or delays is high. Elderly often live alone and there are no witnesses to the attacks. There may be cognitive disorders or other conditions that hinder the collection of the anamnesis; falls and incontinence can sometimes be erroneously related to the attacks. Table III shows some conditions that can lead to diagnostic errors, and the role of instrumental exams is indicated.

A detailed medical history is necessary, possibly supplemented by the testimony of witnesses, a detailed history of the use of drugs or alcohol intake, a general clinical and metabolic balance; a cardiology study, possibly with a dynamic ECG, or with stimulation manoeuvres, is often essential. The usually lesional etiology of seizures requires an accurate neurological examination of the patient and f neuro-radiological examinations. Nevertheless, sometimes it is not possible to obtain assurance that a critical episode was

**Table II.** Classes of drugs reported as possible causes of seizures (from LICE - SIMG Guidelines, [https://www.lice.it/LICE\\_ita/documenti\\_LICE-SIMG/pdf/FARMACI\\_AE\\_e\\_INTERAZIONI.pdf](https://www.lice.it/LICE_ita/documenti_LICE-SIMG/pdf/FARMACI_AE_e_INTERAZIONI.pdf)).

Class of drugs	Molecules
Opiate analgesics	Tramadol, morphine, pentazocine
Anti-asthmatics	Theophylline, salbutamol
Antibiotics	Cephalosporins, fluoroquinolones, erythromycin, penicillins, gentamicin
Antidepressants	Tricyclics, SSRI, bupropion, mianserin, trazodone, venlafaxine
Antimalarials	Chloroquine, mefloquine
Antineoplastics	Busulfan, cisplatin, chlorambucil, methotrexate, vinblastine, vincristine
Antipsychotics	
• typical	Haloperidol, chlorpromazine, fluphenazine
• atypical	clozapine, olanzapine, risperidone
Antihistamines	Chlorphenamine, diphenhydramine
Antivirals	Acyclovir
Cardiovascular	Digoxin, beta-blockers (metoprolol, propranolol), quinidine, disopyramide, mexiletine
NSAIDs	Diclofenac, ibuprofen, indomethacin, ketoprofen, naproxen, piroxicam
Drugs of abuse	All, in particular ethanol and cocaine
Immunosuppressants	Azathioprine, corticosteroids, cyclosporine, interferon-A, tacrolimus
Hypoglycemic agents	Chlorpropamide, glipizide, insulin
Sympathomimetics	Amphetamines, ephedrine, phenylephrine
Others	Baclofen, cimetidine, cycloserine, dantrolene, desmopressin, disulfiram, domperidone, erythropoietin, fampridine, flumazenil, probenecid

NSAIDs: Non-steroidal anti-inflammatory drugs.

**Table III.** Differential diagnosis of epileptic seizures in the elderly.

Terms	Definition	Differential diagnosis
Syncope	Abrupt, transient and complete loss of consciousness associated with loss of postural tone caused by a sudden failure in cerebral perfusion, with rapid and spontaneous recovery	It may be related to cardiac causes (asystole, arrhythmias, structural heart diseases such as aortic stenosis), autonomic control deficits (orthostatic hypotension), nervous reflexes (vasovagal syncope, carotid sinus disease). Syncope involves loss of consciousness and fall with possible traumas, similar to generalized seizures. Subtle myoclonic seizures or brief tonic contractions are possible if the cerebral hypoperfusion is protracted; there is frequently incontinence. The differential diagnosis with a generalized epileptic seizure is based on the accurate collection of history (prodromes, conditions and modalities of onset, presence or absence of post-critical confusion, etc.), ECG and Holter-ECG, and arterial pressure (orthostatic changes) evaluation. In selected cases the study of the vegetative nervous system and the Tilt-test are indicated *
Transient ischemic attacks (TIA)	Focal neurological deficit of short duration (not exceeding 24 h), reversible, from ischemia in the carotid or vertebro-basilar territory	Paralysis after a hemispheric seizure (Todd's palsy) can complicate the differential diagnosis. Physical examination, EEG and neuroradiological examinations can contribute to the diagnosis
Recurrent falls	Unexpected or apparently inexplicable falls are frequent in the elderly, correlated with multiple possible causes	They require a careful anamnesis, in particular for the possible concomitance of disorders of consciousness, and an accurate neurological examination. Consider the possibility of drop-attacks, sudden episodes of fall, with a conserved conscience, related to sudden loss of postural tone, in the absence of signs of posterior circulation dysfunction. They typically especially occur in middle-aged women who fall unexpectedly walking and only rarely standing, often with difficulty in getting up ^
Transient global amnesia (TGA)	Prolonged episodes (hours) of anterograde amnesia in the absence of altered consciousness or confusion	During the episode the autobiographical memory is preserved, but the patient is unable to reap new memories. The contribution of a witness is therefore essential for the diagnosis. Exclude the use of benzodiazepines or alcohol ingestion! Rarely semiologically overlapping episodes are of epileptic nature (Transient Epileptic Amnesia, TEA) §. Diagnostic criteria are a generally shorter duration of critical episodes, the tendency to repeat, the coexistence of other clinical symptoms and epileptic abnormalities on EEG. According to some A. it represents a specific epileptic syndrome in the elderly patient
Sleep disorders	Particularly frequent in the elderly are the confusional awakenings, the behavioral disorder of the REM sleep ("REM behavior disorder", RBD), the nocturnal myoclonus and the restless legs syndrome	RBD is a parasomnia of REM sleep characterized by violent motor behaviors; when awakened the subjects are aware of the fact that they were having vivid dreams. RBD is due to impairment of normal pathophysiological mechanisms that block muscle activity in REM sleep
Non-epileptic psychogenic episodes	Non-epileptic critical episodes on psychogenic basis can occur at any age and in both sexes	Often for the differential diagnosis – particularly delicate when real epileptic seizures coexist – a video-EEG examination is necessary. The acquisition of a "domestic" movie can also be of great importance

\* Shen W-K, Sheldon RS, Benditt DG, et al. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope. *Heart Rhythm* 2017;14:e155-e217;^ Parry SW, Kenny RA. Drop attacks in older adults: systematic assessment has a high diagnostic yield. *J Am Geriatr Soc* 2005;53:74-8; § Bilo L, Meo R, Ruosi P, et al. Transient epileptic amnesia: an emerging late-onset epileptic syndrome. *Epilepsia* 2009;50:58-61.

of epileptic nature, and it must be limited to observation over time (*wait and see*).

The EEG assessment must take into account the possibility of physiological changes in elderly and the possible presence of unusual variants without pathological significance. Prolonged monitoring, both

outpatient and video-EEG, is a tool of considerable diagnostic value, still underused in the elderly. The possibility of easily acquiring "domestic" films with the help of devices now commonly used can often provide a decisive contribution to the differential diagnosis of critical episodes.



## TREATMENT OF EPILEPTIC SEIZURES IN THE ELDERLY

The choice and management of therapy with antiepileptic drugs is a particularly delicate topic in the elderly<sup>2,21,23</sup>. The main problems can be summarized as follows:

- 1 as a physiological consequence of the aging process, there is an increased sensitivity to drugs:
  - even if changes in liver function cannot be demonstrated, the overall metabolic activity is altered with aging<sup>24,25</sup>;
  - similarly, there is an overall reduction in renal function with a decline in glomerular filtration, a decrease in tubular secretory function, a decrease in renal blood flow;
  - changes in body composition, and in particular a reduction in total body water which, together with the reduced drug-protein binding caused by the reduced production of hepatic albumin, can also significantly reduce the volume of distribution of strongly water-soluble and strongly bound drugs such as gentamicin, digoxin, and theophylline. In such cases, the loading dose should be reduced;
  - changes in neurotransmitters and brain receptors, such as decreased choline-acetyltransferase, acetylcholine and serotonin receptors, enzymes involved in the synthesis of GABA/glutamic acid, dopamine levels, also associated with changes in receptor affinity and signal transduction mechanisms.
- 2 the elderly population is frequently exposed to polytherapy (antidepressants, antipsychotics, tranquilizers, hormones, anticoagulants, cardiology drugs, anti-hypertensives, etc), with the possibility of pharmacokinetic and pharmacodynamic interactions, not always perfectly predictable. Faught et al.<sup>26</sup> have recently evaluated the risk of pharmacokinetic interactions between Anti-epileptic drugs (AEDs) and other molecules, and the factors associated with risk in elderly.

General strategies should foresee<sup>23</sup>:

- monotherapy. If this still represents the gold standard in epileptology, it is a priority in the elderly;
- to simplify all therapies as far as possible;
- to know the pharmacokinetic mechanisms of the different drugs used, the possible interactions, and to pay attention to their prediction. Many of the new AEDs are probably less involved in pharmacokinetic interactions and may therefore represent a more appropriate choice in the elderly<sup>26</sup>;
- to monitor, when appropriate, plasma levels of AEDs, in order to prevent their toxicity;

- often the information reported by the manufacturers on the drug doses and speed of titration are not appropriate for the elderly, which presents a marked variability, often not predictable, of drug pharmacokinetics and pharmacodynamics. The advice is to start with low doses, and to proceed with slow and gradual increases (*start low and go slow*).

The choice of the most appropriate drug is a complex problem, and many parameters need to be taken in consideration, including both the characteristics of epilepsy and of the patient as well. Nowadays, about 25 AEDs are available; a list of current AEDs and their suggested mechanism of action is reported in Table IV<sup>27</sup>.

Regarding the specific drug choice, it is easier to indicate those that should be avoided than to give indications based on reliable evidence for recommendation. About adverse effects on the CNS, and possibly on other organs, anti-epileptic depressants such as phenobarbital and benzodiazepines should be avoided; the pharmacokinetic interactions, and the high binding to plasma proteins make the use of phenytoin not very advisable.

Wide spectrum of effectiveness, good tolerability, modest pharmacokinetic interactions and the possibility of rapid titration make valproate one of the possible therapeutic options. In view of the frequency of partial seizures in the elderly, carbamazepine (CBZ) is a particularly used drug, however with caution and slow titration due to possible idiosyncratic effects, possible interactions (eg, with anticoagulants) and for the possibility of skin rashes; therefore the more favourable kinetics, the reduced potential of enzyme induction and the better tolerability of oxcarbazepine (OXC) seem to suggest the latter as one of the first-line drugs in the elderly. OXC also requires special attention to the risk of hyponatremia, which is more frequent than with CBZ, a risk to which the elderly population is particularly exposed, particularly if taking diuretic therapy.

Relatively few randomized controlled trials specifically designed for the elderly population are available, and essentially they involve some new antiepileptic drugs. One study compared lamotrigine (LTG) and CBZ, demonstrating approximately similar efficacy but greater tolerability of LTG, which was therefore proposed as a possible first choice<sup>28</sup>. Moreover, the differences are reduced or cancelled if the comparison was made with the CBZ controlled release rather than with the standard formulation. Another randomized double-blind study compared LTG, gabapentin and CBZ. Once again, the efficacy was approximately equal, with better tolerability for lamotrigine<sup>29</sup>.

**Table IV.** Current antiepileptic drugs and suggested mechanism of action.

Mechanism of action	Antiepileptic drugs
Mainly decrease excitation by blocking sodium channels ( <i>Na+</i> channel blockers)	Phenytoin, fosphenytoin <sup>^</sup>
	Carbamazepine, oxcarbazepine, eslicarbazepine
	Lamotrigine
	Zonisamide <sup>*</sup>
	Lacosamide ( <i>slow inactivation</i> )
	Rufinamide <sup>§</sup>
Mainly decrease excitation by acting on glutamate receptors	Felbamate <sup>*§</sup>
	Topiramate <sup>*</sup>
	Perampanel
Mainly decrease excitation by acting on calcium channels	Etosuximide ( <i>T-type Ca channels</i> )
	Gabapentin, pregabalin ( <i>alfa2-delta Ca subunits ligands</i> )
Mainly decrease excitation binding to the synaptic vesicle protein SV2A	Piracetam <sup>^</sup> , levetiracetam <sup>*</sup> , brivaracetam <sup>*</sup>
Increase GABA mediated inhibition	Phenobarbital, Primidone
	Valproate <sup>*</sup>
	Vigabatrin
	Tiagabine
	Benzodiazepines ( <i>clobazam, clonazepam, diazepam <sup>^</sup>, midazolam <sup>^</sup></i> )
Increasing inhibition by opening KCNQ2-5 channels	Retigabine (ezogabine)
Acting by pharmacokinetic interaction	Stiripentol <sup>§</sup>

<sup>\*</sup>: Multiple, complex mechanisms of action; <sup>^</sup>: for parenteral emergency use; <sup>§</sup>: use restricted to specific conditions (*orphan drugs*).

A double-blind pilot study demonstrated the efficacy of topiramate in the elderly already at 50 mg/day, suggesting the use of medium-low doses, in particular in monotherapy, in this age group <sup>30</sup>; however, the possible negative impact of this drug on cognitive functions must be kept in mind. Open-label studies also support the use of LTG <sup>31</sup>, OXC <sup>32</sup>, levetiracetam (LEV) <sup>33</sup>, zonisamide and lacosamide <sup>34</sup> in the elderly. However the impact of epilepsy and its treatment on cognitive functions, behaviour and mood, and, more in general, on the elderly quality of life, often already compromised, is a topic of considerable importance that should be adequately investigated with specifically designed studies <sup>35</sup>. Recently new AEDs have entered the market. Two of these, brivaracetam and eslicarbazepine (ESL) represent the evolution of the previous drugs LEV and OXC, with possible advantages in terms of efficacy, tolerability, pharmacokinetics and compliance <sup>36</sup>. Moreover, ESL seems to positively affect serum lipid profile, in contrast to the negative impact observed with older carboxamides <sup>37,1</sup>.

Another drug, perampanel (PER), presents a new mechanism of action, since it is a non-competitive highly selective AMPA receptor antagonist <sup>38</sup>. Sub-group analyses derived from controlled studies, and, subsequently, real life studies support the indication of these drugs in the population aged 65 or over <sup>39,40</sup>.

## CONCLUSIONS

Epileptic seizures and epilepsy in the elderly represent, and will represent even more in the future, a significant medical, social and economic problem. The differential diagnosis is not always simple and requires more than ever a careful anamnesis and, in relation to the usually lesional aetiology, a prudent use of instrumental examinations. The frequency of epilepsy, and the high risk of mortality or disability that accompany this condition require a rapid and effective treatment of this neurological emergency. Acute symptomatic seizures require rapid recognition and treatment of the underlying pathology.

Epilepsy in the elderly generally responds positively to drug treatment. However the choice of the drug is conditioned by several factors characteristic of the elderly, including the modified metabolic conditions and sensitivity to antiepileptics, the higher exposure to neurological adverse effects, the frequent comorbidity and the concomitant polytherapy. Some controlled trials seem to favour the use of specific new generation antiepileptic drugs as first choice. In any case, therapy simplification (monotherapy, drugs with simple kinetics) and caution (low doses, very gradual increase, attention to adverse effects and possible drug interactions, repercussions on cognitive performance) must be general criteria to adopt. Last but not least, correct

information and adequate support for the patient are important. The involvement of general practitioners and geriatricians, and of course the family and caregiver, is essential in the effective management of this condition.

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