INTRODUCTION

Altered mental status (AMS) in the elderly have numerous causes with significant morbidity and mortality. In fact elderly patients usually suffer from comorbidities, and require more time and resources than younger ones.

The Emergency Department (ED) is the interface between community and health care institution, and AMS, being a complex symptom, is one of the major challenge for the emergency physician.

The first step consists in the patient evaluation, aimed at determining the cause of the complaints. The differential diagnosis for altered mental status is broad and includes:

• trauma;
• metabolic disorders;
• endocrine abnormalities;
• cerebrovascular accidents;
• seizure.

Confusion and altered mental status are common problems in ED, and ictal confusion, particularly if protracted, is often a diagnostic challenge. Behavioural and mental state disturbances are common but often challenging problems in elderly patients, because seizures may present with nuances that are unique to this age group.

Nonconvulsive status epilepticus (NCSE), an important, and reversible cause of acute confusion, is a possible explanation and probably is frequently missed. The elderly patient with altered mental status pose a difficult diagnostic challenge to the emergen-
Sudden altered mental state in the elderly is a medical and neurological emergency that has been associated with significant morbidity and mortality. SE occurs more frequently in individuals older than 60 years, and the morbidity and mortality of SE are significantly greater in this age group.

On the basis of another widely used classification, based solely on the presence or absence of convulsions, SE can be divided, from an operational and clinical viewpoint, into two main entities (Figure 1):

- convulsive SE (CSE);
- non-convulsive status epilepticus (NCSE).

NCSE is characterised by behavioural or cognitive change from baseline for at least 30 minutes with EEG evidence of seizures. The main categories of NCSE are:

- complex partial status epilepticus (CPSE);
- absence status epilepticus (ASE).

Sustained or recurrent change from baseline behaviour or mental status should be clinically evident. A physician unfamiliar with this kind of patients may not be able to differentiate baseline cognitive and behavioural functions from ictal behavioural and mental state changes. As previously underlined, the detection of this disease may be particularly arduous in elderly subjects, and therefore, a high level of suspicion is essential to obtain an early diagnosis. NCSE is the ultimate condition in which the disciplines of neurology and psychiatry meet and, at times, overlap. Diagnosis is often delayed and mistaken for delirium, stupor, or other causes of confusion.

**Figure 1**

Classification of status epilepticus based on the presence or absence of convulsions

- **Status epilepticus (SE)**
  - Situation longer than 30 minutes of continuous seizure activity or two or more sequential seizures without full recovery of consciousness between the seizures.

- **Convulsive status epilepticus (CSE)**
  - Similar to NCSE, but with a predominant motor component.

- **Non convulsive status epilepticus (NCSE)**
  - Range of conditions in which electrographic seizures activity is prolonged and results in nonconvulsive clinical symptoms.

- **Complex partial status epilepticus (CPSE)**
  - Status that usually presents focal discharges and is considered the equivalent of prolonged or repetitive complex partial seizures.

- **Absence status epilepticus (ASE)**
  - Status characterised by generalised spike and slow wave discharges.
NCSE is an epileptic condition lasting >30 minutes in which continuous or recurrent seizure activity on the electroencephalogram (EEG) is responsible for diverse clinical symptoms including impairment of consciousness, abnormal behaviour or perception disturbances [4]. It requires EEG for confirmation.

Agitation in younger patients accessing the ED is much more likely to be the result of substance abuse or underlying psychiatric disease (psychotic or mood disorder), than in the elderly population. Post-ictal confusion may last as long as 1-2 weeks in an elderly patient, as opposed to minutes in younger individuals. Moreover, many elderly people have medical illnesses that can cause clinical deficits similar to NCSE, leading to the risk of misdiagnosis. NCSE is under-recognised, particularly in patients who have abnormal baseline cognitive abilities or multiorgan medical illnesses. However few studies have exclusively assessed NCSE in the elderly, and NCSE may be diagnosed incorrectly as metabolic abnormalities or psychiatric conditions. NCSE has been increasingly diagnosed given the higher index of suspicion and recent advances in long-term EEG monitoring among patients with impaired level of consciousness.

Neurology of the older adult thus demands a more holistic and multidisciplinary approach: distinguishing normal age-related changes from those that require treatment is a challenge. Altered mental status should not be attributed to psychiatric causes until a careful history and evaluation have pointed out other aetiologies. The purpose of this article, therefore, is to describe some of the major principles of the diagnosis of NCSE in the elderly, in contrast to NCSE in younger patients. Geriatric assessment, multidisciplinary teams, observation units and geriatric ED have been described and tested to manage elderly ED patients or to shift them towards alternative care sources. Even experienced physicians may not made the exact diagnosis during the whole course of the patient’s stay in the ED, despite using all possible means including laboratory and imaging studies. Physicians who develop expertise in recognising these nuances will make more timely diagnoses and be less likely to miss the diagnosis. Neurologists are ideally placed to manage SE, particularly those with a knowledge of EEG, and should be consulted early.

**Characteristics of NCSE in the Elderly**

The geriatric population is at special risk for mental alterations for a myriad of reasons. The most common cause of AMS in order of frequency are:

- multifactorial causes;
- medications;
- infections;
- metabolic disorders;
- trauma;
- neoplasm;
- cardiovascular diseases;
- dehydration;
- nutritional abnormalities;
- seizure (epilepsy).

Unfortunately, there is only a limited number of articles about the diagnosis of AMS in the ED.

In the following paragraphs, I will use “nonconvulsive status epilepticus” (NCSE) as a descriptive term denoting cases of SE with little or no clinical signs of ongoing seizure activity apart from obtundation or subtle motor phenomena.

NCSE has a heterogeneous presentation, is commonly underdiagnosed, and early detection and treatment require a high level of suspicion. It consists of changes in basal mental status (confusion or depressed level of consciousness) for at least 30 min and EEG evidence of continuous or almost continuous epileptiform activity. Slight motor manifestations may be seen, such as eyelid myoclonia, automatisms, nystagmus, or discrete extremity dystonia, in the absence of evident convulsive activity [5].

There is no universally accepted definition of NCSE. In a consensus workshop organised by the Epilepsy Research Foundation (amid at facilitating communication and research in this area), it has been defined as “a term used to denote a range of conditions in which electrographic seizure activity is prolonged and results in non-convulsive clinical symptoms” [6].

In general, NCSE differs from CSE in the lack of a predominant motor component [7]. The definition of NCSE preferred by Shorvon is “nonconvulsive status epilepticus is a term used to denote a range of conditions in which electrographic seizures activity is prolonged and results in nonconvulsive clinical symptoms” [8].
The two types of NCSE have different features: absence SE (ASE) is characterised by generalised spike and slow wave discharges, while complex partial SE (CPSE) usually presents focal discharges and is considered the equivalent of prolonged or repetitive complex partial seizures (Figures 2 and 3).

Absence status was reported to occur de novo in later life as a situation-related, single event.

ASE may be considered those cases similar to «status epilepticus in petit mal» described by Schwab [9].

CPSE is NCSE with a presumed focal onset.

CPSE was reported less often than absence SE until recently, perhaps because of some very stringent definitions. Clinical manifestations include an «epileptic twilight state» with a lack of responsiveness or confusion, and bizarre, and particularly fluctuating, behaviour [10,11]. Most recently, a classification proposed by the International League Against Epilepsy (ILAE) has subdivided focal NCSE (focal; CPSE) into aura continua (non-convulsive simple partial SE with maintained consciousness) and dyscognitive SE (with impaired consciousness) of mesial temporal or neocortical origin. While the forms originating from the mesial temporal lobe regions may be summarised as “limbic status” manifesting with limbic sensations, the manifestations of the neocortical forms reflect the region of origin involved [12].

As stated in the Introduction, both the incidence and prevalence of epilepsy are high among the elderly. The incidence of SE has a bimodal distribution, with the highest incidences during the first year of life and after the age of 60 [13]. Among adults, patients older than 60 had the highest risk of developing SE, with an incidence of 86/100,000 persons per year [14–16].

NCSE may constitute one quarter of all SE in patients over 60 years old, and up to 40% of all SE occurs in the elderly. Today the estimated frequency of NCSE is around 32–85 cases/100,000/year [5]. Older adults' increased risk for stroke, metabolic abnormalities, and comorbid conditions contributes to the frequency of seizures in this population.

Cerebrovascular disease is the most commonly identified cause of SE in the elderly and accounts for the majority of NCSE. About 7% of acute strokes provoke at least one epileptic seizure, and about one fifth of these result in SE, sometimes nonconvulsive [17]. Tumours and traumas may each account for another 5 to 10% of NCSE [18]. Neurodegenerative disorders in adults are progressively recognised as one of the major causes of epilepsy. Many of the remainders are multifactorial [19,20].

A history of seizures is not always present, nor is motor activity necessarily associated with NCSE. Primary generalised “absence” seizures occur in the elderly, usually after an earlier epilepsy diagnosis [21], or with de novo absence SE of late onset – often following benzodiazepine or other medication withdrawal, even without earlier epilepsy [22]. NCSE can be precipitated by several toxic, metabolic, and epileptic triggers. Triggering factors for situation-related ASE in the elderly are protein, including psychotropic and other seizure precipitating drugs such as aminophylline, benzodiazepine withdrawal, metabolic imbalance, systemic infections and fever, alcoholism and dehydration [23].

With an increasingly ageing population, and age itself being an independent risk factor for stroke, the incidence and prevalence of post-stroke seizure and post-stroke epilepsy are likely to increase. Cerebrovascular disease is the most common underlying cause, although as many as 25–40% of new epilepsy cases in the elderly have no obvious underlying aetiology [24].

Most NCSE in the elderly are not primarily generalised but of focal onset, complex partial status (CPSE), with possible secondary generalisation. Older patients were more likely to have focal discharges, again indicating that NCSE in the elderly tends to be “symptomatic” or arise from a focal lesion [18,25,26]. The term “symptomatic” indicates that the seizure activity is a secondary phenomenon or a symptom of an underlying disease process.

Almost 75% of patients older than 40 are women [27,28], and ASE over the age of 50 is predominantly a female disorder [29]. Globally, NCSE appears to have a worse prognosis in the elderly (NCSE mortality in elderly patients ranges up to 57% [30]), with more severe underlying processes including infections [31].

The mortality rates for SE, which are not uniform across age groups, are about 40% for patients aged older than 60 years and exceed 60% for those older than 80 [32,33].

The use of a classification based on the age at which NCSE occurs has recently been suggested [5,34]. Rare neuropathologic
case reports have described neuropathologic changes associated with SE in humans [35,36]. This correlates with neuronal loss within the hippocampus, especially in the CA1 and CA4 regions, as well as neuronal loss in more diffuse brain regions [37].

Important differential diagnoses of NCSE are:
- metabolic encephalopathy;
- migraine aura;
- posttraumatic amnesia;
- prolonged post-ictal confusion;
- psychiatric disorders;
- substance de- or intoxication;
- transient global amnesia;
- transient ischemic attack [38].

From an electroencephalographic point of view, a clear development with a build-up of rhythmic activity or generalised spike-wave discharges at 3 Hz or faster and decremental features with flat periods associated with clinical seizure activity strongly indicate NCSE [39].

THE SPECTRUM OF THE CLINICAL FEATURES OF NCSE IN THE ELDERLY

As previously noted, NCSE diagnosis is difficult, due to its heterogeneous presentation, which is undistinguishable from other causes of altered awareness: its clinical manifestations can include the full spectrum of mental status changes; patients may only show subtle clinical signs of seizure activity such as mild myoclonic movements; and presentation is very inconsistent, varying in intensity from mild personality changes, such as drowsiness and difficulty in concentration, lethargy, agitation, blinking, confusion, facial twitching, automatisms, to severe manifestations such as coma [40]. Since all the symptoms may be improved by treatment, some investigators consider the clinical and electrographic response to antiepileptic drugs, especially benzodiazepines, an important aspect for the diagnosis of NCSE. However, the response to these medications may not be immediate, occurring many days after the beginning of the treatment, precluding its inclusion among major diagnostic criteria [41].

Behavioural disturbances related to these confusional states (confusion in the elderly, language disturbances, cortical blindness, confabulation, psychotic states, sensory phenomena, autonomic disturbances and psychic phenomena. In one larger series of patients with NCSE seen in emergency rooms, agitation, lethargy, disruptive behaviour, mutism or other language disturbances, delirium, staring, oral automatisms, inappropriate laughter or crying, rigidity, and several other types of bizarre behaviour were presenting signs [44].

Thomas et al. noted that status could be present from 8 hours to 5 days before being diagnosed, and described clinical features such as «interrupted speech, catatonia, slow and ataxic gait». Many of the elderly patients diagnosed with NCSE have not had epilepsy...
Sudden altered mental state in the elderly

DIAGNOSTIC APPROACH TO NCSE

Clinical examination

The number of accesses to Emergency Departments has substantially increased during the past few years, especially for patients aged 65 years and older.

The ageing of the general population is a well known trend. By the year 2020, it is estimated that, every second, one person in Germany will be older than 50 years old, and some 7% of the population will be 80 or older [51]. The US government predicts that by 2030 there will be 70 million adults over age 65 in the United States. Whereas this segment made up 12.4% of the population in 2000, it will account for about 20% by 2030 [52].

Furthermore, current demographic trends will lead to an increased prevalence of epilepsy in the general population, leading to the necessity of a major effort aimed at improving our understanding of the clinical course and optimal treatment of epilepsy in this rapidly growing segment of the population.

Unfortunately, there are documented problems with the quality and continuity of care provided to older ED patients, including failure to recognise problems that could benefit from more careful assessment, failure to refer to appropriate community services, and failure to timely communicate to the primary physician the problems identified and interventions implemented at the ED visit. This may represent a consistent problem in the management of acute mental change, which must be evaluated in rapid sequence or simultaneously while using the tools of basic resuscitation, history, clinical assessment, laboratory evaluation and radiological assessment.

A tool that can help in reminding the reasons why a patient can show an altered mental status is common mnemonic called AEIOU-TIPS (Table I).

Table I
Meaning of the mnemonic AEIOU-TIPS

<table>
<thead>
<tr>
<th>A</th>
<th>Alcohol, other toxins, drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>Endocrine, electrolytes</td>
</tr>
<tr>
<td>I</td>
<td>Insulin, diabetes-related, hypoglycaemia</td>
</tr>
<tr>
<td>O</td>
<td>Oxygen, opiates</td>
</tr>
<tr>
<td>U</td>
<td>Uremia</td>
</tr>
<tr>
<td>T</td>
<td>Trauma, temperature</td>
</tr>
<tr>
<td>I</td>
<td>Infection</td>
</tr>
<tr>
<td>P</td>
<td>Psychiatric, poisoning, porphyria</td>
</tr>
<tr>
<td>S</td>
<td>Stroke, poisoning, shock, subarachnoid haemorrhage</td>
</tr>
<tr>
<td>M</td>
<td>Metabolic: hyperammonia</td>
</tr>
</tbody>
</table>

earlier in life but have had benzodiazepine withdrawal or other significant effects of medications on the brain [22]. Visual hallucinations and visual loss similar to those of migraine can be an unusual manifestation of focal NCSE [45]. Catatonia [46] and atonia [47] have been described as manifestations of NCSE. Speech difficulties due to dysarthria rather than aphasia can be caused by SE arising in the opercular regions [48].

NCSE presenting as a progressive aphasia that developed insidiously over 5 weeks has been described [49]. There are often severe language disturbances, with mutism and verbal perseveration. Frequent features are bizarre behaviour, agitation, aggressiveness, emotional liability, and hallucinations [50]. Occasionally automatisms such as chewing and compulsive handling of objects have been noted, and on examination, frontal release signs and a Babinski reflex have been documented [50].

Furthermore, it may become especially difficult to diagnose CPSE (dyscognitive SE) in elderly patients in whom it is as frequent as of 40%. In fact, as already remarked in this article, the differentiation of this type of dyscognitive SE from nonepileptic conditions without EEG and by pure clinical means may become challenging even for the skilled epileptologist.

Typical psychiatric manifestations of dyscognitive SE include delirium, stupor or catatonia, mental slowing, cognitive decline, aggressive behaviour and psychotic depression. When spreading to the neocortical areas of the temporal lobes, auditory or visual hallucinations may occur. The EEG of dyscognitive SE is characterised by irregular or regular focal spikes or spike-wave activity similar to the one observed in aura continua; however, the ictal activity in dyscognitive SE tends to involve a larger area which increases the likelihood to detect it by surface EEG [12].
diagnosis is often delayed and appropriate intervention may not be initiated. The diagnosis of NCSE is important because it is potentially reversible. It is difficult to treat this pathology appropriately if the diagnosis does not come to mind.

Certain clinical features that are more likely to be present in patients in NCSE compared with other types of encephalopathy (e.g. waxing and waning state of prolonged seizures, unassociated with major motor activity such as convulsions). Either remote risk factors for seizures or ocular movement abnormalities were seen in all patients in NCSE. If these typical features are present, an EEG urgently be performed [55].

**Electroencephalographic evaluation**

The definite diagnosis of NCSE is dependent on electroencephalographic confirmation. Electroencephalographic and videoelectroencephalographic studies performed while the patient is experiencing symptoms are crucial to early diagnosis and timely management [56].

Since NCSE in the elderly is of focal onset [18,25,26], neuroimaging can be taken into consideration in order to identify any underlying structural abnormalities. The hallmark of NCSE is a change in behaviour or mental state that is associated with diagnostic EEG changes. EEG evaluation is vital to confirm the diagnosis of NCSE and may also be useful to exclude other potential explanations for the clinical signs, such as metabolic disorders, infections of the nervous system, transient ischaemic events or in the case of syndromes whose clinical presentation is dominated by behavioural and psychiatric symptoms.

A number of EEG patterns have been described in NCSE, and many of these are controversial, particularly if they are ictal. There seems to be agreement that the overall picture of the electroencephalographic discharge and its evolution in time and space is helpful in differentiating the electroencephalography of encephalopathies from that of NCSE. The EEG findings of NCSE are heterogeneous; generalised or focal (temporal, temporo-frontal) spike-and-wave complexes, polyspike discharges, irregular sharp or slow waves may be seen. A clear development with a build-up of rhythmic activity or generalised spike-wave discharges at 3 Hz or faster and decremental features with flat periods associated with clinical seizure activity strongly indicate NCSE [39]. In ambulatory patients, the most common EEG patterns associated with NCSE are generalised spike-and-wave or generalised polyspike-and-wave discharges in the case of ASE, or rhythmic focal discharges in the case of CPSE [57]. Absence status and focal NCSE can be distinguished easily by EEG, the former being characterised by generalised 2 to 4 Hz spike and wave activity and the latter by more or less focalised discharges generally associated with the temporal or frontal lobe.

In perhaps the best study of the EEG in NCSE, Granner and Lee evaluated NCSE patients who responded well to antiepileptic drugs [26]. NCSE patients who responded well to antiepileptic drugs EEG discharges were often generalised, but many became focal once the medication has been initiated. The researchers found a wide variety of different alterations such as typical or atypical spike wave discharges, multiple or polyspike wave discharges, and also rhythmic delta activity with some spikes. Waveform morphologies were remarkably variable; discharge frequencies were generally from 1.0 to 3.5 Hz (mean 2.2). Most of these changes appeared to be generalised but some were focal.

In NCSE, ongoing seizure activity, whether focal or generalised, with clearly defined spike-slow-wave discharges usually more than 2 Hz, often waxing and waning, is usually diagnostically straightforward [30]. The EEG borderlands of what represent seizures versus what are postictal or interictal patterns, periodic epileptiform discharges (PEDs), and triphasic waves (TWs), have been the subject of some study with incomplete consensus. PEDs have been referred to as an “irritative” pattern found in temporal proximity to seizures proper, the footprints rather than the animal itself [58].

The clinician should look for signs that would point to potential localisations of a brain disturbance such as focal paresis, focal sensory deficits, or aphasia. In parallel, it is a good idea to look for signs of conditions that could produce symptoms that mimic seizures, but are not seizures, for example irregular heart rates or cardiac murmurs suggesting the risk of syncope. In order to put the patient’s presentation into the proper context, a careful medical history should be taken and standard laboratory tests performed to exclude other possible diagnoses.

I suggest making the diagnosis of the NCSE only if, in addition to the electro-
TREATMENT

Treatment focuses on correcting underlying pathologic abnormalities such as hyponatremia or drug toxicity, and initiating pharmacologic therapy.

From a clinical point of view, the treatment of NCSE in the elderly population is complicated by several major factors such as altered pharmacokinetics (i.e. altered drug metabolism and excretion) and comorbidity, related to the risk of interaction with concomitant medications. In treating epilepsy, the choice of antiepileptic drug (AED) is usually dictated by seizure type and tolerability and maybe complicated by comorbidities or age-associated differences in AED pharmacokinetics. The objective should be complete control of seizures, with enhanced quality of life.

Treatment of NCSE in the elderly is strikingly easy in some and impressively difficult in others. The choice of AED should focus on avoidance of side effects and adverse drug-drug interactions. Patients with primary generalised, absence SE usually respond to modest doses of benzodiazepines and often do not need long-term AED maintenance. CPSE is typically due to some underlying lesion and often requires long-term medication. CPSE has a mortality of approx. 30% in the elderly, simple partial SE 40%, and generalised status 90% [25]; many of the patients with generalised NCSE are those mentioned earlier with severe medical and neurological illnesses and prolonged electrographic SE. The treatment of NCSE needs to be tailored to the perceived urgency and morbidity of the condition.

Because prognosis varies depending on the causes, and may be a by-product of the morbidity conferred by the inciting brain insult, some experts advocate oral or intramuscular treatment, or supplementation with antiepileptic; others recommend careful monitored use of iv benzodiazepines [30]. The benzodiazepines are considered the first line treatment for both ASE and CPSE [59]. The initial recommended treatment consists of intravenous diazepam or lorazepam. If seizures persist, a loading dose of phenytoin or fosphenytoin is subsequently given. Blood pressure and cardiac rhythm must be monitored continuously during a rapid infusion, and if adverse effects occur, the infusion rate should be slowed.

CONCLUSIONS

AMS remains a symptom that carries a significant degree of morbidity and mortality, especially in elderly patients with neurological aetiologies (in the elderly 22-39% of AMS are secondary to medications [60]). NCSE, as a complex of symptoms, is and will remain one of the major causes of access to ED. It represents a pleomorphic condition of patient without overt convulsions [30].

Although relatively frequent, NCSE is a poorly understood and under-diagnosed condition. NCSE should be suspected whenever cases of fluctuating consciousness or abrupt cognitive or behavioural changes are noted. The often unspectacular and unspecific clinical manifestation of NCSE makes it important to “think of it at all” in any patient presenting with unexplained new onset of behavioural changes, impaired consciousness and/or focal, non-convulsive neurological deficits [61].

NCSE is one of the most important neurological emergencies requiring rapid diagnosis, being confirmed by EEG and treated without delay and with appropriate aggressiveness.

Finally, elderly patients with confusion should undergo diagnostic EEG, particularly if the confusion is episodic or there have been previous episodes of protracted ictal confusion. If EEG is not performed during the symptomatic period, the diagnosis is likely to be missed.

More research is needed to determine the effectiveness of screening and intervention strategies targeting at-risk older ED patients. Future research should be targeted to investigate and manage this symptom complex.

DISCLOSURE

The Author declares that he has no financial competing interests.
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