



## Review

# The role of electroencephalography in the early diagnosis of non-convulsive status epilepticus in elderly patients with acute confusional state: Two possible strategies?

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## ABSTRACT

Non-convulsive status epilepticus (NCSE) can pose considerable diagnostic challenges, especially in the elderly, because of the wide differential diagnosis with common underlying causes of acute confusional state in this age group. We reviewed the proposed electroencephalography (EEG) strategies to improve the diagnostic yield of non-convulsive status epilepticus in the elderly population. Specifically, a debated topic of clinical relevance is the exact role of the EEG in the early diagnosis of NCSE in the elderly. Two EEG strategies have been proposed to improve the diagnostic yield of NCSE: emergent abbreviated EEG (EAEEG) recordings with reduced montages, and continuous EEG (CEEG) monitoring. Both approaches appear to be potentially advantageous, but at the same time subject to intrinsic limitations. Our literature review found initial evidence that the diagnostic yield for NCSE of prolonged EEG recordings is superior to routine EEGs. Further research is needed to confirm these preliminary findings and to explore strategies to improve the feasibility of a more widespread use of prolonged recordings within acute clinical settings.

## 1. Introduction

Non-convulsive status epilepticus (NCSE) is a challenging, albeit potentially reversible, neuropsychiatric condition characterised by non-convulsive clinical manifestations with alterations in the conscious state ranging from mild confusion to coma, and abnormal brain electrical activity (as recorded by electroencephalography, EEG) [1–3]. In 2013, the Salzburg consensus statement promoted the use of a unified EEG terminology and proposed working diagnostic criteria for NCSE [4–12]. The incidence of NCSE has been estimated to increase with age: 15.5/100,000 in the 60–69 age group, 21.5/100,000 in the 70–79 age group, and 25.9/100,000 in patients aged 80 and older [13]. However, the recognition of NCSE in the elderly can be particularly challenging, as a wide range of differential diagnoses of acute confusional state need to be considered in this population [14,15]. Overall, NCSE might be one of the most frequently missed diagnoses in elderly patients presenting

with altered mental status, because of its broad range of presentations, significant co-morbidities (especially cerebrovascular disease), limited awareness of this particular seizure emergency and/or difficulties with access to EEG [16–18].

In consideration of the central role of EEG in the diagnosis of NCSE [19,20], it is important to keep a high index of suspicion for NCSE in any case of fluctuating encephalopathy, with a low threshold for requesting an emergent EEG to evaluate the possibility of underlying epilepsy as a possible reversible cause [21]. However, clinicians working in emergency departments and general district hospitals often have to deal with limited access to neurophysiology services when assessing acutely confused elderly patients. Plans to introduce more flexible EEG assessment tools accessible within the emergency department have recently been implemented in order to fill this diagnostic gap: despite early positive results, these investigational strategies are far from reaching widespread use [22]. Moreover, direct access to EEG

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facilities in clinical settings with temporally and spatially limited recordings may introduce the potential for false negative findings [23]. It would be useful to evaluate the available evidence on the optimization of the use of emergent EEG in the assessment of elderly people with acute confusional state caused by an underlying epilepsy that may be masked by common co-morbidities. We therefore conducted a literature review to assess the role of emergent EEG in the pathway to a prompt and accurate diagnosis of NCSE in the elderly.

## 2. Methods

We carried out a narrative review of the available literature on the role of emergent EEG in the diagnosis of NCSE in the elderly. The following inclusion criteria were adopted: 1) original studies on elderly individuals, defined for the purpose of this review as aged 60 or older; 2) studies on elderly patients with ACS or similar clinical conditions presenting with altered consciousness and/or behaviour; 3) studies with focus on the prevalence and clinical correlates of NCSE in elderly patients with ACS; 4) studies published in English language. Exclusion criteria were as follows: 1) studies on patients diagnosed with coma; 2) studies on patients with focal status epilepticus without impairment of consciousness; 3) studies published as single case reports. Three scientific databases (MEDLINE, EMBASE, PsycInfo) were searched using the terms “NCSE”, “elderly”, “EEG”, “emergent EEG”, “urgent EEG”, “diagnosis”, “confusion”, as well as their derivations. In order to ensure that no relevant studies were missed out, an additional search for NCSE and EEG regardless of age limits was undertaken. Finally, the reference lists of the articles retrieved through the outlined search strategy were manually screened and the Google Scholar database was searched for grey literature meeting the above criteria.

## 3. Results

NCSE is a dynamic condition with aetiological and pathophysiological features that mimic and overlap with delirium and encephalopathy, often posing a diagnostic challenge in elderly patients with acute confusional state. Although EEG investigations are deemed to be essential in reaching a diagnosis, there are uncertainties about the timing and the modality of using the EEG in order to minimise the risk of overlooking NCSE. Few studies [23–26] have explicitly focused on the prevalence of EEG features that are compatible with NCSE in elderly patients with acute confusional state. However, the high heterogeneity of the patient selection criteria and the different methodologies of these studies limit the possibility of comparing their findings and drawing definite conclusions.

Overall, two different and conceptually opposing strategies with relative variants on the same theme have been suggested in order to avoid missing a potentially reversible diagnosis such as NCSE. Emergent abbreviated EEG (EAEEG) recordings with reduced montages have been proposed and contrasted with continuous EEG (CEEG) monitoring. Both approaches appear to be potentially advantageous, but at the same time subject to intrinsic limitations (Table 1).

**Table 1**

Proposed electroencephalography strategies to improve the diagnostic yield of non-convulsive status epilepticus.

Emergent abbreviated EEG		Continuous EEG	
Advantages	Disadvantages	Advantages	Disadvantages
Ease of use	Limited sensitivity	Increased sensitivity	Not feasible for agitated and confused patients
No requirement for highly specialized personnel to set up equipment	Requirement for highly specialized personnel to interpret recording	Ability to capture variable and dynamic changes associated with NCSE	Requirement for highly specialized personnel to set up equipment and interpret recording
Potential screening tool to patients with acute confusional state			Time consuming and draining on limited resources

Abbreviations. NCSEnon-convulsive status epilepticus; EEGelectroencephalography.

The use of EAEEG can be implemented at an earlier stage and out of hours without the need for highly specialized personnel, thus theoretically intercepting a higher number of cases of NCSE in a more timely fashion, so as to allow prompt treatment interventions, although probably at the cost of reduced sensitivity. Conversely, CEEG monitoring has been associated with an increased diagnostic yield, but may be prove more challenging in agitated and dysphoric patients, who require the presence of dedicated and specialized personnel for the duration of the recording procedure.

Bautista [27] advocated the use of an abbreviated (5-minute) EEG in the early assessment of patients with changes of the mental status of unknown cause. Specifically, he found that EAEEG may assist in differentiating between NCSE and encephalopathy in the diagnostic work-up of patients with acute mental changes. A short and user-friendly EEG setting had previously been explored and proved to have high sensitivity (96%) in diagnosing epilepsy when compared with standard telemetry [28]. However, Kolls and Husain [29] warned against the use of a quick and easy screening hairline EEG to rule out NCSE, since they found it to have low sensitivity, failing to identify seizures with more benign patterns. According to Bubrick et al. [30], it would be inappropriate to dismiss outright the usefulness of this test when applied in clinical contexts where there is a strong suspicion of NCSE and a longer recording time could be obtained. A study by Bubrick et al. [31] focused on the use of abbreviated, emergency below-the-hairline EEGs (BTH-EEG) performed in patients with altered mental status by neurology residents when no EEG technologist is available. Their findings showed that, in selected cases, BTH-EEG is useful in detecting seizures and/or other epileptiform patterns: when NCSE was suspected, abnormal EEG patterns were detected by BTH-EEG in 41% of the cases. More recently, Muraja-Murro et al. [32] described the performance of a user-friendly disposable forehead EEG electrode set suitable for EAEEG recordings and compared its use against routine 10–20 system full-head scalp electrode EEG in 100 consecutive acute neurological patients (53 women; age range 18–90 years) with unexplained altered mental state who underwent investigations to rule out SE. The forehead EEG missed two cases because the EEG findings supporting the diagnosis of SE were localised to the posterior areas of the brain and the authors concluded that, with a forehead EEG set, the NCSE detection rate was 50%, whereas the specificity was 100%. Overall, this was considered to be an acceptable trade off, as it can help to avoid the delay associated with the need for trained technicians and equipment set-up. However, the interpretation of EEG findings that are consistent with NCSE proved challenging and relied on the expertise of clinical neurophysiologists, who tend to be a rare resource in most settings, especially on an on-call basis.

In summary, there are a few practical objections to the widespread use of EAEEG: 1) potentially limited sensitivity, as EAEEG devices can only record activity from part of the scalp; 2) availability of recording devices that allow for temporally and spatially limited traces; 3) need to train staff who are not specialists in neurophysiology. Moreover, although a rapid and easy EEG recording can be obtained, the acquired data have to be adequately reported, and an expert interpretation may

not be as immediately available [29]. It has been proposed that wireless systems allowing remote access for reviewing by neurophysiologists may provide a feasible solution and indicate the future direction to pursue [33,34]. Alternatively, the use of EAEEG could be better suited for highly selective cases: this view was endorsed by Brenner et al. [35], who implemented the use of a bedside reduced-montage EEG to confirm the diagnosis of NCSE in patients with a known history of seizure or a witnessed seizure. In this study, the diagnostic process required the input of a board-certified epileptologist, who provided the interpretation of the recordings via telemetry.

An opposite approach to the diagnosis of NCSE involves the use of CEEG monitoring. A study by Rai et al. [36] showed that short-term EEG is ineffective in detecting seizures in critically ill patients with altered sensorium, and should not be used as substitute for long-term EEG. Likewise, a subsequent study by Mesraoua et al. [37] showed that CEEG monitoring is an essential tool in detecting NCSE in patients with altered mental status. The potentially superior diagnostic yield of prolonged EEG recordings was explored more fully in a study by Naeije et al. [23], who retrospectively reviewed 15 CEEG recordings performed in elderly patients (aged over 75 years) with acute confusional state who had undergone routine EEGs. The authors found that, when baseline EEGs were non-contributory, CEEG recordings identified interictal epileptiform discharges in two cases and NCSE in one case. Conversely, among patients with no epileptic abnormalities or interictal epileptiform discharges only on baseline EEGs, CEEG recordings revealed nonconvulsive seizures in one case and NCSE in three cases. Although this study was a retrospective analysis of a small group of selected patients with acute confusional state in whom no convincing alternative aetiology for their clinical presentation was identified, the main findings were supportive of the superiority of CEEG recordings in detecting epileptic events in elderly persons with acute confusional state. The authors also pointed out that NCSE or non-convulsive seizures occurred at least 30 min after the recording in three out of the five cases and would have probably been missed by simply repeating a routine EEG. The same authors [26] replicated these findings in a subsequent prospective study, where two homogeneous groups of patients aged over 65 years with a diagnosis of delirium were assessed using either baseline EEG or CEEG. CEEG recordings detected patterns compatible with NCSE in 28% of cases, whereas routine EEG detected patterns compatible with NCSE in only 6% of cases. The only significant difference between the two groups was a significantly higher history of epilepsy in the group of patients who underwent CEEG: 4/32 or 13% versus 1/32 or 3% ( $p$  value 0.039). This difference might at least partially explain the study results, since an history of epilepsy is regarded as a risk factor for the development of NCSE and SE [38,39]. However, NCSE can often present with features of agitation, aggressivity, violent behaviour, and hallucinations [40,41], which may undermine the practicality of performing CEEG recordings: patients may not be compliant, especially when confused and agitated. Specifically, patients may move excessively, producing muscle and movement artefacts that can hamper the interpretation of the EEG recording. Only the first one of the two studies by Naeije et al. [23] explicitly mentions the absence of any significant technical issues. Overall, the presence of normal routine EEG in elderly with acute confusional state was deemed insufficient to dismiss the suspicion of NCSE and the presence of interictal epileptiform discharges in baseline recordings was strongly suggestive of concomitant non-convulsive seizures or NCSE, which could be confirmed using prolonged recordings.

#### 4. Discussion

There appears to be insufficient evidence to establish evidence-based criteria for the prioritization of urgent EEG in elderly patients with suspected NCSE; thus, a low threshold for obtaining an EEG should be maintained for elderly persons with fluctuating encephalopathy. Since EEG plays a central role in the diagnosis of NCSE, the

optimization of EEG protocols in the emergency setting would be an important achievement. Although EEG is known to have high sensitivity in detecting epileptic abnormalities, routine EEG recordings may fail to adequately capture a dynamic and variable electroclinical phenomenon such as NCSE. Continuous EEG monitoring may be more promising in terms of increasing the diagnostic yield, however there are practical limitations related to resource allocation and availability, as some emergency departments can barely afford routine (let alone continuous) EEG recording. In addition to obtaining the EEG recording, expert neurophysiological review of the EEG data is crucial in view of the variable features that electrographic discharges may assume in NCSE. The correct interpretation of EEG findings is further complicated by the existence of multiple EEG mimics, such as periodic abnormalities, that resemble epileptic activity. It has only recently been suggested that the term epileptiform should be dropped for generalized and lateralized periodic discharges, as these EEG patterns may be an epiphenomenon of structural or metabolic disorders and are not necessarily linked to epileptic activity. These EEG patterns should be differentiated from epileptic discharges with clear spatiotemporal evolution or a periodicity with higher frequency (above 2.5 Hz), which are likely to reflect ongoing seizure activity confined to specific regions or spreading over both hemispheres.

Faster, user-friendly and simplified EEG applications have been proposed to meet the needs of busy emergency departments, although their sensitivity might be inferior to more traditional recording protocols. Again, there is a need for skilled EEG reading and interpretation by experienced neurophysiologists who are aware that routine EEG offers only a limited temporal window on the functional fluctuations of abnormal brain activity. Moreover, NCSE is known to be a continuously evolving condition, not just clinically but also electrographically. In this context, research efforts aimed at identifying elderly patients with acute confusional state at higher risk for developing NCSE are needed to achieve evidence-based prioritization strategies for urgent EEGs. Future research should also be conducted to develop neurophysiological protocols that can improve the diagnostic process of NCSE in the elderly, including extended EEG [42] and, in selected patients, video-ambulatory EEG [43]. This latter has been shown to be particularly useful in complex clinical scenarios, such as the diagnosis of epileptic and non-epileptic seizures [44,45]. An open question is how to deal with elderly confused patients in whom NCSE is highly suspected but no EEG is available at all on admission. From an organizational perspective, it is advisable that neurological facilities are conveniently located and readily accessible to acute admission units. Neuropsychiatric input might also prove invaluable in the longer term. Finally, other diagnostic tools have been reported to be potentially useful in supporting the diagnosis of NCSE when EEG findings are not available or unable to capture deep abnormal electrical activity. A study by Kutluay et al. [46] showed that ictal/subtraction ictal SPECT can be a useful complementary noninvasive diagnostic investigation in patients with focal NCSE, when the EEG findings are suspicious but inconclusive. Other diagnostic techniques that have been shown to potentially have a complementary or supplementary role in the diagnosis of NCSE include computed tomography perfusion [47] and the sodium amytal test [48].

#### 5. Conclusions

In the absence of reliable clinical predictors of NCSE, it is important to keep the threshold for requesting EEG relatively low in elderly patients with acute confusional state, even in the presence of a presumed symptomatic cause. Repeat EEG assessments may increase the diagnostic yield and help to identify a treatable and reversible condition such as NCSE. A currently debated topic of clinical relevance is the exact role of the EEG in the early diagnosis of NCSE in the elderly. Specifically, two possible strategies have been explored in clinical studies: ‘short and easy’ (EAEEG) or ‘long and cumbersome’ (CEEG). Our literature review found initial evidence that the diagnostic yield for

NCSE of prolonged EEG recordings is superior to routine EEGs. Further research is needed to confirm these preliminary findings and to explore strategies to improve the feasibility of a more widespread use of prolonged recordings within acute clinical settings.

## Declaration of Competing Interest

None.

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