



## Review article

# EEG criteria for diagnosing nonconvulsive status epilepticus in comatose - An unsolved puzzle: A narrative review

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## A B S T R A C T

**Introduction:** Nonconvulsive status epilepticus (NCSE) is an important and often unrecognized cause of impaired awareness especially in critically ill patients, which can easily be missed. Electroencephalography (EEG) findings in clinically suspected cases are the mainstay of diagnosis.

**Review summary:** The EEG diagnostic criteria for NCSE have evolved over the past three decades. Furthermore, recent advancements in EEG technologies such as continuous EEG monitoring, and emergency department EEG, along with development of different diagnostic criteria, have increased the detection rate for NCSE in suspected cases. However, treating physicians should have a higher index of clinical suspicion and a lower threshold for recommending this valuable investigation. The introduction of different diagnostic criteria has made it easier for electroencephalographers to report NCSE; nevertheless, diagnosis is not always straightforward. This narrative review aimed to define and discuss the available literature on different EEG diagnostic criteria for NCSE.

**Conclusion:** There is a need for further prospective research to strengthen the diagnostic accuracy of the available diagnostic criteria, the modified Salzburg Consensus Criteria for NCSE (mSCNC) and updated American Clinical Neurophysiology Society (ACNS) 21 criteria, to verify their accuracy to detect NCSE in comatose patients.

## 1. Introduction

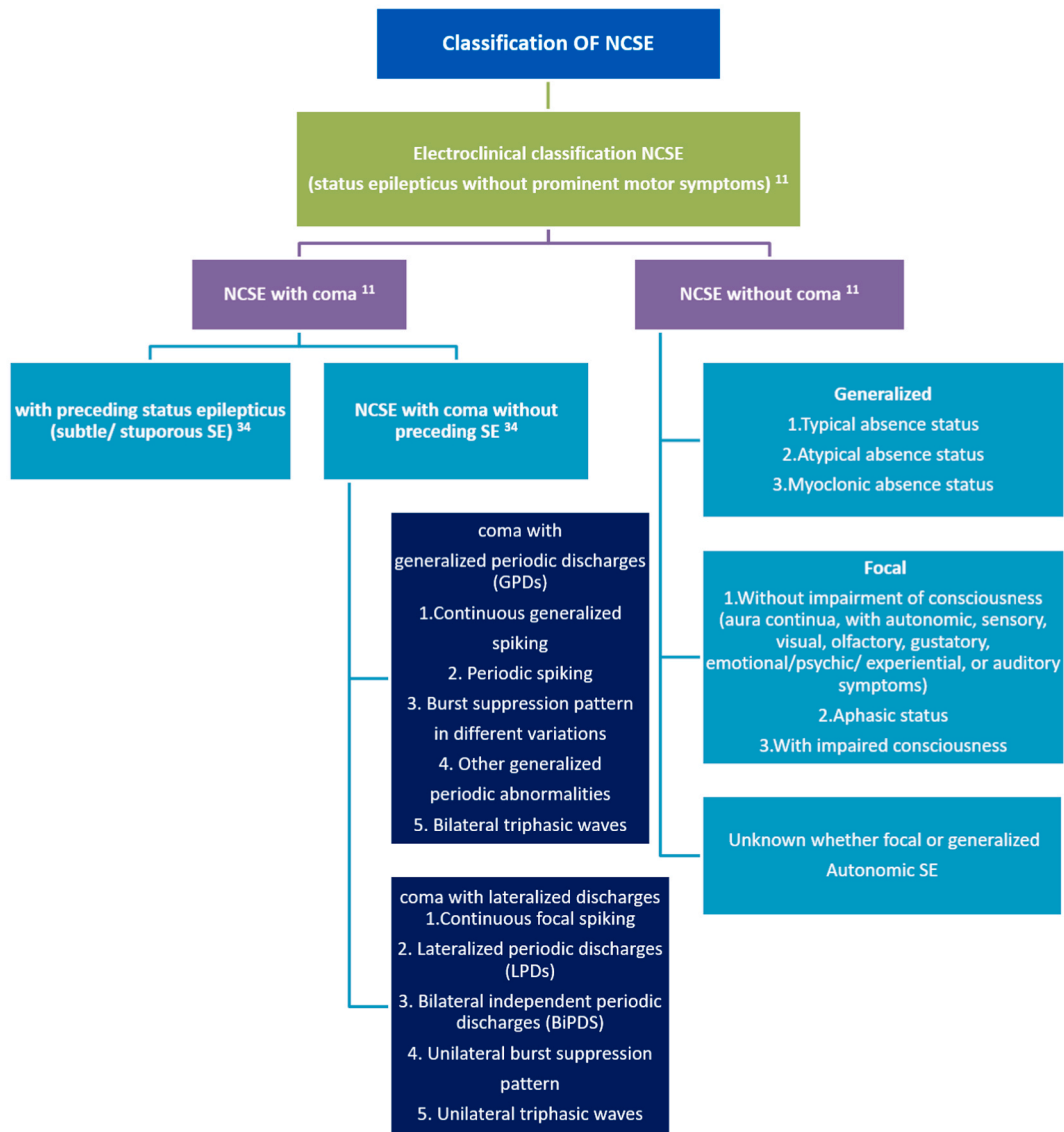
Nonconvulsive status epilepticus (NCSE) is an important but often undiagnosed entity of status epilepticus (SE) because of its lack of overt clinical manifestations. Furthermore, its varied manifestations may result in diagnoses other than seizures [1]. Recognition of subtle clinical features and supportive EEG findings are the main diagnostic tools for detecting these cases [2]. Although, NCSE lacks convulsive activity, it causes significant neuronal injury. Hence, its recognition and treatment are crucial [3].

NCSE is an important cause of altered consciousness levels in critically ill patients admitted to the intensive care unit (ICU) or emergency department. In the ICU setting, reported frequency of NCSE ranges between 8 % and 48 % [4–8]. Moreover, it is occasionally detected incidentally while EEG is performed to evaluate delirium or encephalopathy in patients without any history of epilepsy [9].

The mainstay of diagnosing NCSE is an electrographic seizure (ESz) and electrical status epilepticus (ESE) detected on EEG in the presence of clinical suspicion. In settings where EEG is not available, documented clinical improvement (CI) in a close temporal relationship with antiseizure medications (ASM) also suggests NCSE. However, the absence of such a clinical response does not exclude the diagnosis [10]. NCSE is broadly divided into proper and comatose forms [11]. In the past 20 years, various refinements in the definition and EEG diagnostic criteria have been proposed to make the diagnosis of comatose NCSE easier. Among the different diagnostic criteria, the Salzburg Consensus Criteria for NCSE (SCNC) have recently been proposed and validated for diagnostic

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**Fig. 1.** Classification of non-convulsive status epilepticus (NCSE); adopted from the International League Against Epilepsy (ILAE) Task Force classification <sup>11</sup> and recommendations from Bauer and Trinka. <sup>34</sup>.

accuracy. This review discusses the EEG features and criteria suggested to diagnose NCSE in adults.

## 2. Definition and description of SE and NCSE with historical background

NCSE denotes an enduring epileptic condition or electroclinical state with an altered or reduced mental state (AMS), behavioral and vegetative abnormalities, or merely subjective features, such as auras, but lacks major convulsive movements [3,12].

Ictal impairment of cognition, fluctuations in the level of consciousness, behavioral changes, subtle twitches affecting the face or limb, head or eye deviation, and automatism are features that suggest the possibility of NCSE. As the clinical manifestations of NCSE are pleomorphic and may often be confused with other conditions, the diagnosis is largely dependent on confirmatory EEG showing seizure activity [2].

Initially, NCSE was not classified as a distinct entity, and SE was defined as prolonged or repeated seizures of undefined duration without returning to the baseline consciousness level – [13–18]. Later, the duration was set to 30 min [19–21], which was further shortened to 20, 10, and finally 5 min [22–24]. Prolonged nonconvulsive seizure (NCS) was included under the umbrella of SE as NCSE by Gastaut et al., in 1967 [25]. Subsequently, many researchers have suggested that changes in the clinical state, often comprising AMS, detection of ESz on EEG, and responsiveness to ASM, should be considered as NCSE [26–29]. Furthermore, an ictal event/ESz for 30 min on EEG was considered as NCSE [30,31].

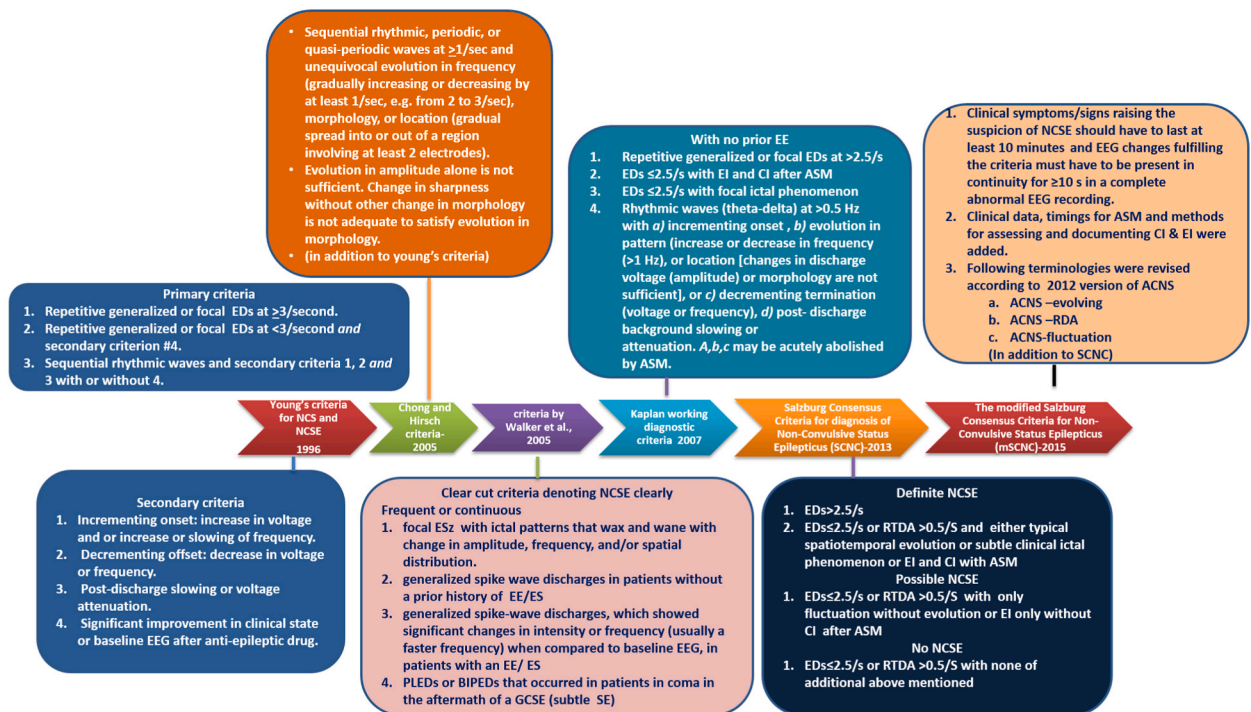


Fig. 2. The evolution of different proposed EEG diagnostic criteria for NCSE.

In 2015, the International League Against Epilepsy (ILAE) task force proposed definitions encompassing all variants of SE while incorporating t1 and t2 time definitions based on its pathophysiology [11]. As limited information was available to define the t1 and t2 dimensions for NCSE [32], Trinka et al. proposed the t1 time dimension as 10 min and t2 as 60 min for focal SE with impaired consciousness. For absence SE, only the t1 dimension was set as 10–15 min [11].

### 3. Classification of NCSE

NCSE is broadly categorized into NCSE proper (NCSE without coma) and NCSE comatose (NCSE with coma) [23]. In 2007, Rossetti et al. used the term “NCSE in coma” synonymously with subtle generalized convulsive status epilepticus (SGCSE) [33].

While NCSE proper has obvious clinical manifestations accompanied by minimal impairment of consciousness, such as the absence status epilepticus, patients with comatose NCSE do not exhibit such features, and the diagnosis depends entirely on EEG findings. In 2010, Bauer and Trinka categorized comatose NCSE into coma with lateralized epileptiform discharges (LED) and that with generalized epileptiform discharges (GED), based on EEG findings. Other forms, including subtle/stuporous SE and *epilepsia partialis continua* (EPC), were categorized as the borderline between NCSE proper and comatose [34].

An axis-based classification for SE was introduced by Trinka et al., in 2015 [11]. The subtypes of NCSE according to this classification are shown in Fig. 1. In this classification, some clinical entities were defined as borderline syndromes owing to their currently undetermined relationship with NCSE. Epileptic encephalopathy (EE), coma with epileptiform EEG patterns without any characteristic evolution such as lateralized periodic discharges (LPDs) and generalized periodic discharges (GPDs) with monotonous appearance, behavioral disturbances in epileptic individuals, and epileptiform EEG patterns in patients with delirium are among some of these borderline syndromes [11].

### 4. The EEG criteria for NCSE

Several attempts have been made to define the EEG characteristics of NCSE without a universally accepted definition. The unsolved dilemma of EEG findings in the absence of apparent clinical seizures and the differences in EEG interpretations by the reader to report NCSE in comatose patients are major concerns to be solved [35].

The different published EEG diagnostic criteria for NCSE in these patients are summarized in Fig. 2.

#### 4.1. Young's criteria for NCS and NCSE, 1996

In 1996, Young et al. [36] proposed EEG diagnostic criteria for NCS or ESz. The authors suggested at least one primary and one or more secondary criteria with discharges lasting for more than 10 s should be considered as ESz [36]. Provided with the definitions of SE

**Table 1**  
Summary of studies evaluating Salzburg Consensus Criteria.

Authors and year of publication	Objective	Number of patients	Results and interpretation
Othman et al., 2020	To evaluate the concordance between the EEG diagnosis of NCSE made by the treating physician and the application of SCNC.	181	A perfect concordance was found for the Definite- and No-NCSE categories. SCNC was found to have an optimal performance for the 'Definite NCSE,' and to exclude the presence of NCSE.
Goselink et al., 2019	To validate the diagnostic accuracy of the Salzburg criteria, using EEG recordings from patients with and without a clinical suspicion for NCSE.	191	The sensitivity of SCNC was 67 % and specificity was 89 % in the validation cohort. The positive predictive value was 47 % and the negative predictive value was 95 %. Specificity was 89.2 % in the control group. The SCNC showed a lower diagnostic accuracy than the original study, suggesting that SCNC cannot replace the practice of careful consideration of both clinical as well as EEG information on an individual basis.
Krogstad et al., 2019	To validate the application of SCNC by a trained junior EEG examiner without the knowledge of previously proposed EEG criteria, against the original diagnosis by an experienced EEG examiner.	284	There were eight false-negatives, one false-positive, 39 true-positives, and 236 true-negatives. Concordance between SCNC and the reference standard was high. The SCNC for NCSE implemented by an inexperienced EEG reader, blinded to all other data, yielded results highly concordant with the evaluation of EEG by an experienced reader.
Tuncer et al., 2018	To assess the usefulness of SCNC for determining the prognosis of critically ill patients with NCSE.	107	NCSE was diagnosed in 33 patients (30.8 %) using SCNC. SCNC were found compatible in clinical setting in making the decision for the treatment of patients with NCSE
Leitinger et al., 2016	To assess the diagnostic accuracy of the Salzburg EEG criteria for NCSE.	220	The sensitivity of SCNC for NCSE was 97.7 % and the specificity was 89.6 %. The overall diagnostic accuracy was 92.5 %. The SCNC for the diagnosis of NCSE was found to have high diagnostic accuracy and excellent inter-rater agreement, which makes it suitable for implementation in the clinical settings.
Leitinger et al., 2015	To test the influence of the ACNS criteria on test performance of SCNC regarding specificity and sensitivity for NCSE in non-hypoxic patients.	100	Implementing the ACNS terminology led to clinically relevant and statistically significant reduction of false positive diagnoses for NCSE and a minimal loss in sensitivity. The modified SCNC with refined definitions was proposed by the authors in contrast to SCNC.

and partial SE and accompanied with impaired awareness at that time, the authors defined NCSE as EEG-recorded continuous ictal discharges or recurrence for >30 min without any CI to baseline level, or return of the EEG recording to a preictal EEG pattern between the seizures.

#### 4.2. Chong and Hirsch criteria, 2005

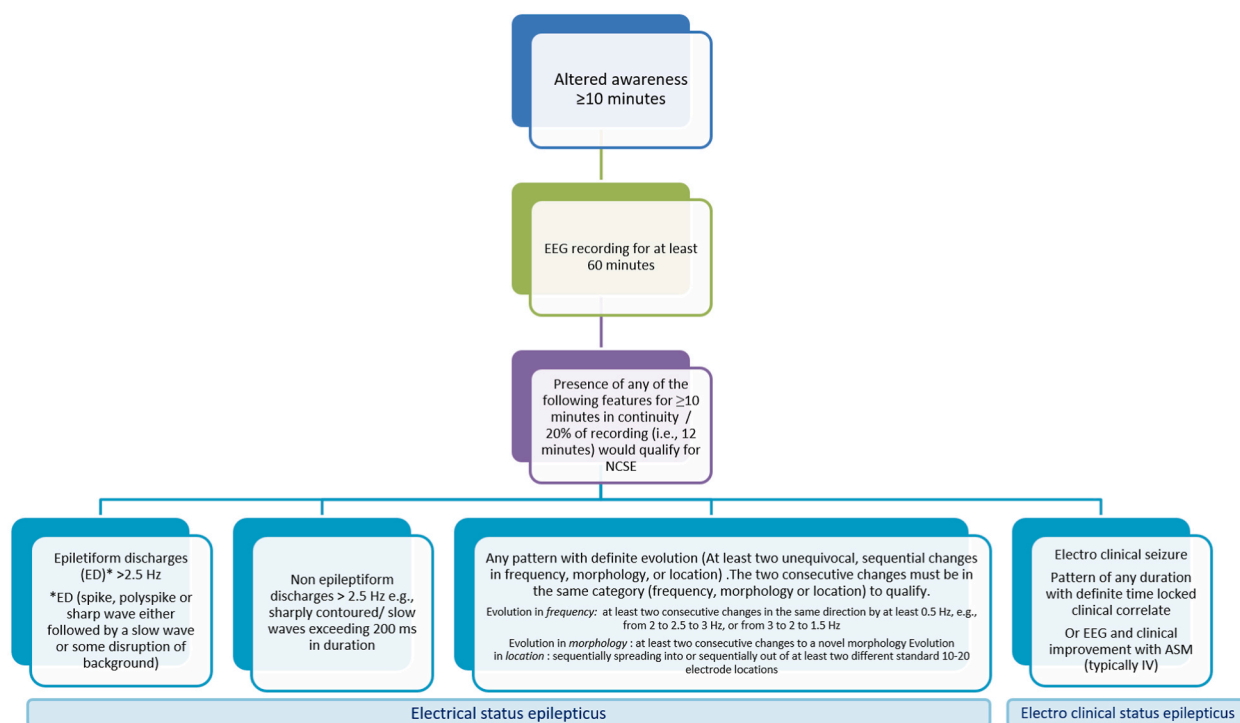
In 2005, Chong and Hirsch [37] made some modifications in the criteria proposed by Young et al. [36] and further refined them for epileptic discharges of <3 per second and sequential rhythmic waves to be considered as ictal patterns on EEG (Fig. 2). The evolution of the amplitude alone was described as insufficient, and change in the morphology or the spatial spread was added. The authors also added that the resolution of epileptiform discharges (EDs), except diffuse slowing without observed clinical improvement or the appearance of previously absent normal EEG patterns, would not satisfy the secondary criterion.

#### 4.3. EEG diagnostic criteria by Walker et al., 2005

In April 2004 [38], a consensus was reached that the diagnosis of NCSE in adults is primarily dependent on electrographic ictal activity. Furthermore, various boundary conditions with electrographic ictal activity and without obvious clinical seizures were included in the NCSE rubric. Based on ESz activity, six criteria were established, among which four were labelled as clear-cut criteria, denoting NCSE clearly, and two as equivocal criteria, denoting NCSE in some cases, as detailed in Fig. 2.

#### 4.4. Kaplan working diagnostic criteria in 2007

Kaplan established working criteria for NCSE in 2007, clearly isolating patients with EE from those without EE and suggesting every detail of electrographic discharges and patterns to be considered NCSE [2]. However, the frequency of discharges to be considered ictal without any additional parameters was set at >2.5 per second.



**Fig. 3.** electrical status epilepticus as defined in 2021 version of ACNS critical care EEG terminology.

#### 4.5. Salzburg Consensus Criteria for NSCE (SCNC), 2013

SCNC were proposed by Beniczky et al. [39]. In SCNC, further refinement was made to Kaplan's criteria, and the diagnosis was simplified by introducing "definite," "possible," and "no" NCSE. However, the evaluation of findings based on the prior presence or absence of EE was retained. In patients with known EE, an increase in the prominence or frequency of EEG features, compared to baseline findings with observable changes in clinical state, was the same as that described by Kaplan<sup>2</sup> to diagnose NCSE. However, improvements in both clinical/CI and EEG features (EI) with intravenous ASM was recommended for the diagnosis of definite NCSE [39].

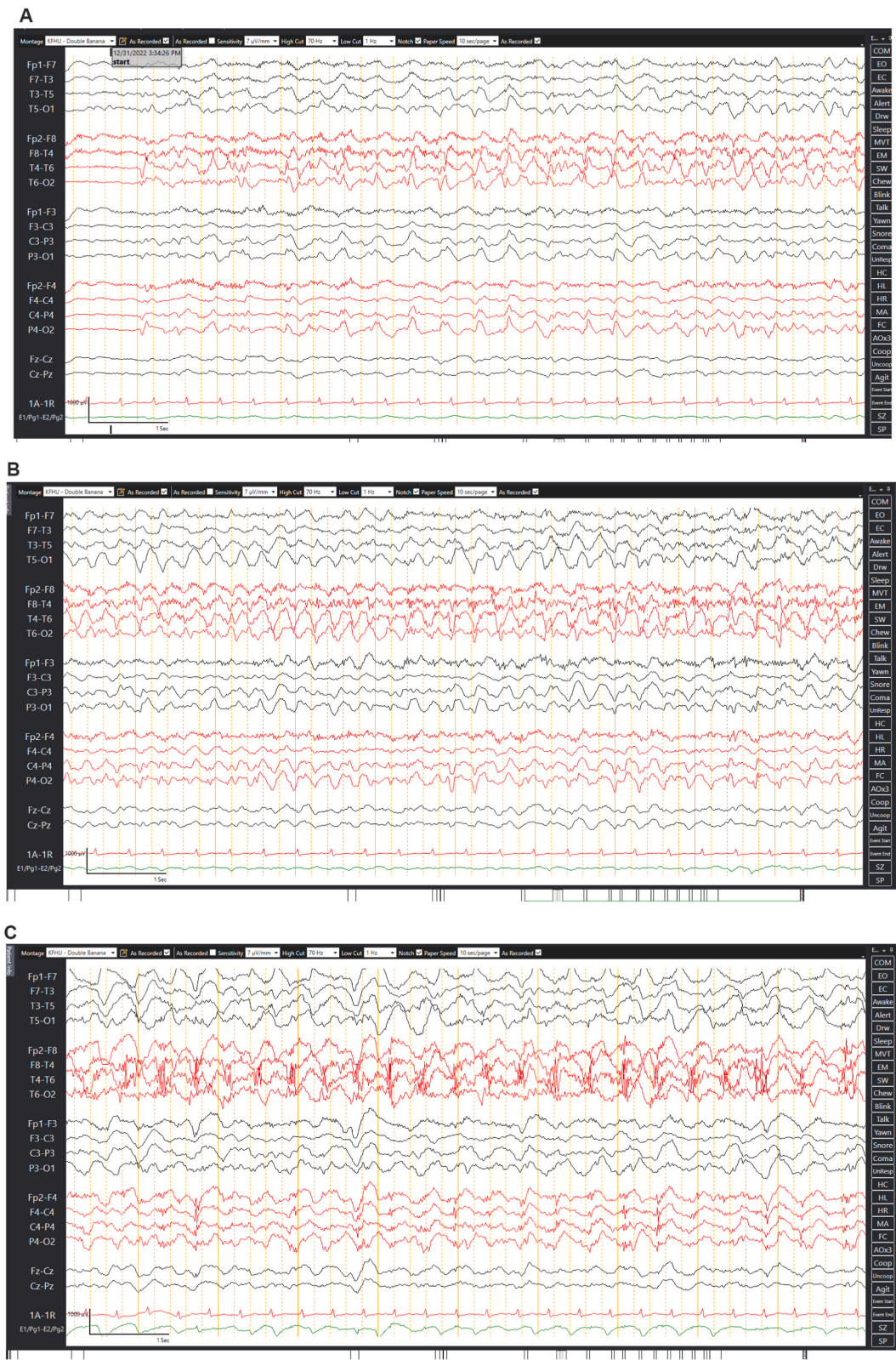
#### 4.6. The modified Salzburg Consensus Criteria for nonconvulsive status epilepticus (mSCNC), 2015

To improve the sensitivity of SCNC and reduce the false positive diagnoses of NCSE, an introduction to the definitions of "evolving" (ACNS-evolving) rhythmic delta activity (RDA) and fluctuation according to the 2012 version for a Standardized Critical Care EEG Terminology by ACNS [40] was provided by Leitinger et al., in 2015 [41]. The authors conducted a retrospective comparative study that included the EEGs of 50 consecutive nonhypoxic patients with NCSE and 50 patients with abnormal EEGs without NCSE. The 2012 ACNS criteria were implemented to strengthen the test performance of SCNC. The authors found that the implementation of ACNS definitions for RDA and fluctuation led to a statistically significant reduction in false-positive diagnoses, and proposed a modified SCNC (mSCNC) for further research purposes.

mSCNC is recommended for all patients with impaired consciousness and suspected NCSE. However, physicians should have clarity regarding the diagnosis of NCSE, which is the result of combining EEG interpretations and clinical information. In mSCNC, it was emphasized that clinical symptoms/signs raising the suspicion of NCSE should last for at least 10 min [11], and the EEG changes fulfilling the criteria must be present in continuity for  $\geq 10$  s in a complete abnormal EEG recording. The required clinical information was also included in the criteria.

## 5. Studies validating SCNC

Criteria must be practically validated in order to implement them. The diagnostic accuracy of SCNC has been evaluated in various studies. Leitinger et al. evaluated the diagnostic accuracy of the SCNC and found it to be suitable for clinical application. The authors found the overall diagnostic accuracy to be 92.5 %. It was concluded that besides improving the diagnostic accuracy in clinical practice, the criteria could be used as an important research tool because they provided precise diagnostic standards for inclusion in therapeutic clinical studies in patients with NCSE [41]. Some researchers objected to the retrospective nature, short duration of EEG monitoring, and performance of the validating study by authors involved in the development of the criteria and discussed their views



**Fig. 4.** example of electrographic seizure with spatio temporal evolution. 4a shows start of ESz as sharp waves in right temporal region, 4b and 4c show evolution in frequency and morphology of epileptic discharges.

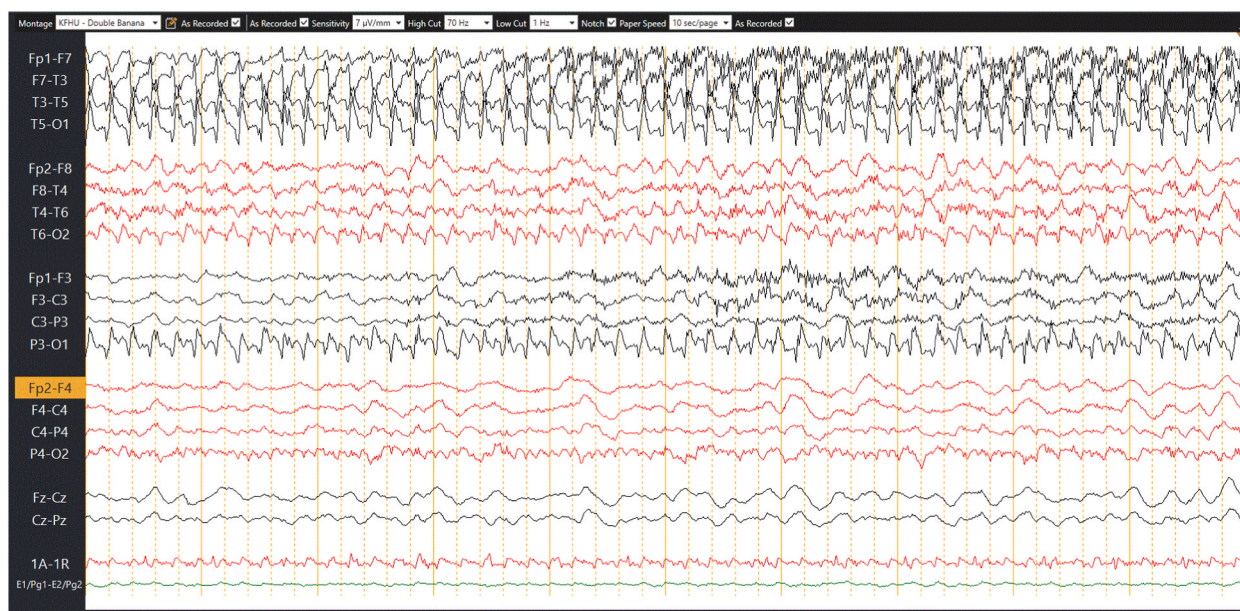


Fig. 5. electrographic seizure with epileptic discharges more than 2.5 per second in left temporal and occipital head region.

[42–44]. Later, these objections were clarified in detail by Leitinger et al. [45]. The duration of a 10 s for an ictal event on EEG to be considered as NCSE has been criticized by different researchers [42,43]. However, the authors clarified that the entire EEG should be abnormal, and clinical information should always be weighed together with an EEG interpretation [41].

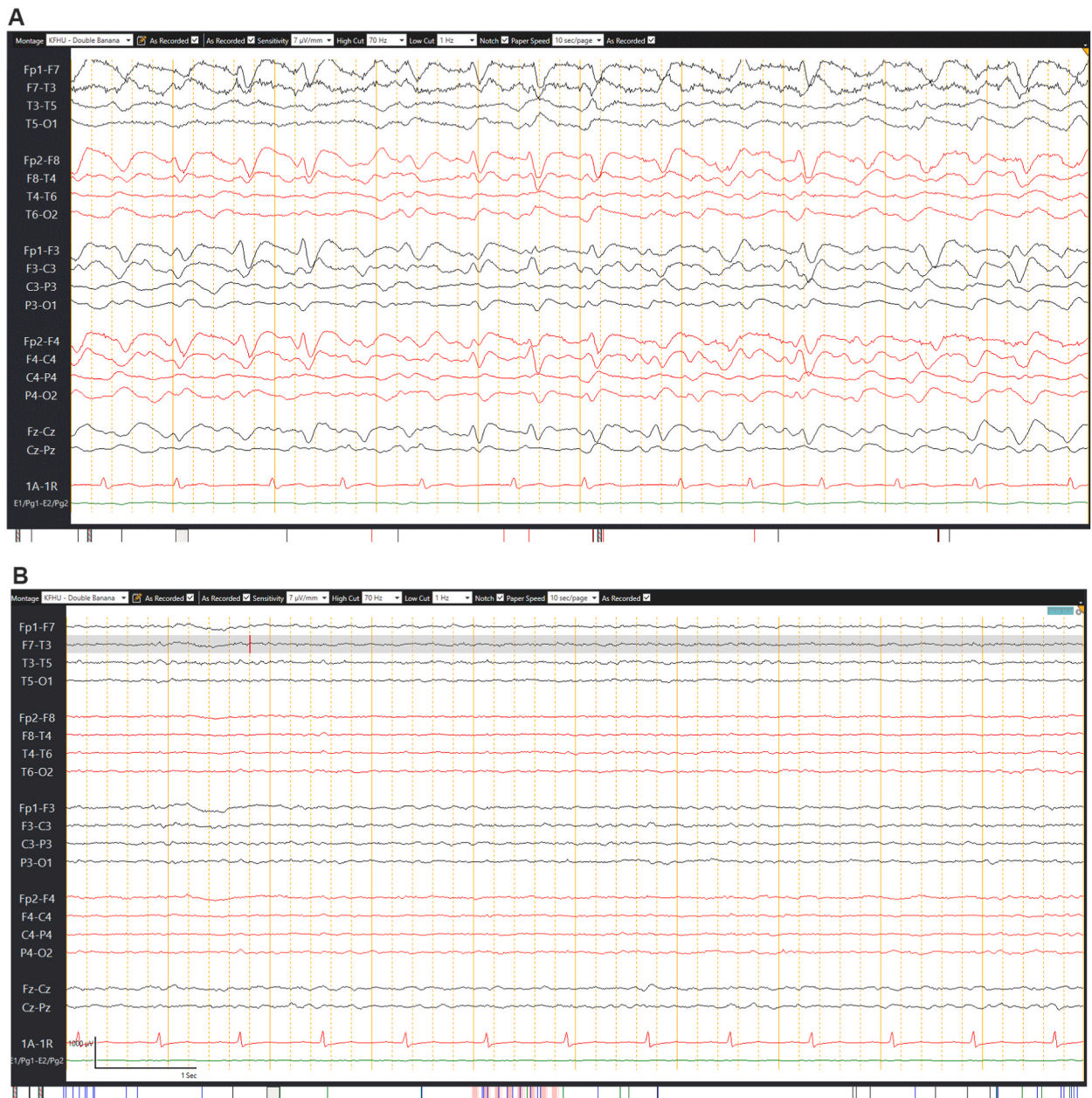
An external validation study found a lower diagnostic accuracy of SCNC for the diagnosis of NCSE compared to the original validation study by Leitinger et al. [41], and the authors inferred that the criteria cannot be automatically transferred to clinical settings where an EEG evaluation for NCSE is warranted [46]. The authors involved in the development of SCNC later explained the reasons for the lower diagnostic accuracy by Goselink et al. [46] compared to the original validation study [41] as a deviation from the published criteria in methodology, and provided clarification for the implementation of additional criteria for patients with EE [47].<sup>47</sup>

In contrast to the study by Goselink et al. [46], other studies found SCNC highly compatible with clinical practice in the decision-making for the treatment of patients with NCSE [48–50]. Studies utilizing SCNC are summarized in Table 1.

## 6. American clinical neurophysiology Society's standardized critical care EEG terminology, 2021 version

Recently, in the 2021 version of ACNS critical care EEG terminology [51], various newer terminologies were added and modified, including ESz and electrical status epilepticus (ESE), depending on the revised ILAE classification for epilepsy [11] and published research data [52,53]. In this revised version, the definition of ESz was adopted from the Salzburg criteria [39,41,51] with some modifications regarding epileptiform discharges [51]. ESE was clearly defined as either having ESz lasting for 10 min in continuity or  $\geq 20\%$  of a 60-min EEG recording. Furthermore, electroclinical seizures (ECSz) and electroclinical status epilepticus were defined clearly [51]. ECSz was described as a pattern of any duration with definite time-locked clinical correlates or EEG and clinical improvement with ASM, preferably intravenous. The term “electroclinical status epilepticus” (ECSE) is used when electroclinical seizures persist for 10 min in continuity or gain, as for ESE, comprising 20% of an hour of an EEG recording. Based on these descriptions, NCSE can be classified as either ESE or ECSE. However, this 12-min time period is based on studies of children [52] and neonates [53], and not adults; therefore, it is still debatable whether physicians should apply this to adults. Furthermore, a 10-min duration was set based on the ILAE definition for focal status epilepticus with impaired awareness [11], and hence, may not be applicable in other forms of NCSE, including NCSE comatose. In contrast to this revised time definition to diagnose ESE (described in Fig. 3) in comatose patients, mSCNC appears to be more likely to diagnose NCSE in comatose. Moreover, SCNC has been validated by several studies. Whether implementation of this new definition by ACNS for ESE is better than mSCNC in detecting NCSE in comatose patients and improving its outcome requires further research. However, it appears that this revised time definition will reduce the chances of diagnosing NCSE in comatose patients and may further delay its management. Examples of ESz and ECSz are shown in Fig. 4 (a–c), 5, 6 (a,b), and 7 (see Fig. 7).

In summary, despite advances in EEG technology, the diagnostic dilemma of NCSE comatose remains. The only validated criteria in studies for the diagnosis of NCSE and SCNC require further prospective research to strengthen their diagnostic accuracy. Based on the revised ACNS criteria, the minimum duration of an EEG recording to detect NCSE should be 60 min. However, many setups still perform 30 min recording. This review summarizes the available EEG diagnostic criteria for NCSE. We emphasize the imminent need for research in the field of epilepsy, implementing updated unified terminologies, definitions, and validated criteria to solve this puzzle. Studies comparing 30 min versus 60 min recordings may help in identifying the minimum time requirement for EEG recording



**Fig. 6.** epileptiform discharges responding to ASM, 6a-sharp waves in bilateral frontocentral head regions in a patient with fluctuating consciousness level and roving eye movements. 6b-disappearance of abnormality 20 s after intravenous midazolam.

to diagnose NCSE. Comparative studies investigating mSCNC versus the revised ACNS version 2021 to diagnose NCSE comatose could help physicians set further timelines.

#### Data availability statement

No data was used for the research described in the article.

#### CRediT authorship contribution statement

**Azra Zafar:** Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Danah Aljaafari:** Writing – review & editing.



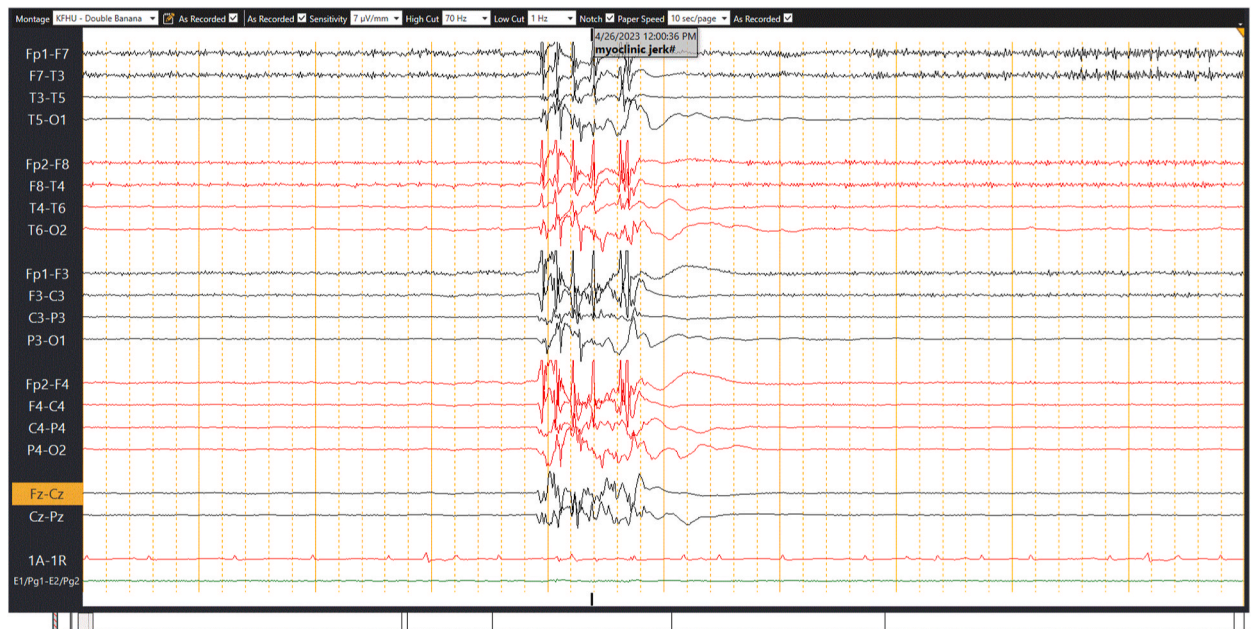


Fig. 7. example of electroclinical seizure. Polyspikes generalized epileptic discharges time locked to subtle myoclonus.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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