Review Article

Continuous EEG monitoring in the evaluation of non-convulsive seizures and status epilepticus

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Non-convulsive seizures (NCSzs) and non-convulsive status epilepticus (NCSE) occur in a substantial proportion of patients with acute brain injury. These acute seizure disorders are often unrecognized and under-diagnosed. Seizure semiology of NCSz is too subtle clinically to be noticed. Most often, mental status impairment is the presenting feature. Changes in the functions of the thalamo-cortical system in patients with impaired consciousness can be detected by continuous EEG (cEEG) monitoring. cEEG monitoring allows detection of the changes at a reversible stage, often when there are no clinical indications of such phenomena. In addition EEG provides reasonable spatial resolution and excellent temporal resolution. This makes cEEG an excellent method for supplementing single or serial recordings in the detection of NCSzs and NCSE. Recent advances in digital EEG have made cEEG monitoring in the neurological intensive care unit (NICU) technically feasible. Current evidence suggests that the common clinical denominator associated with electrographic seizures or NCSzs is mental status impairment. In NCSE, the duration of ictal activity and the time of delay to diagnosis are independent predictors of poor outcome. It will be prudent to do cEEG monitoring in any patient with impaired consciousness either in the setting of acute brain injury or with no clear explanation to detect NCSzs/NCSE. Early recognition and timely intervention is likely to be associated with good outcomes.

Key Words: Non-convulsive seizures, Non-convulsive status epilepticus, Status epilepticus, Electrographic seizures, Electroencephalogram, Continuous EEG monitoring.

Non-convulsive status epilepticus (NCSE) is an under-diagnosed neurological emergency and is defined as mental status changes from baseline of at least 30 to 60 minutes duration associated with continuous or near continuous ictal discharges on electroencephalogram (EEG).[1] Early recognition and timely intervention is likely to be associated with good outcomes.[2] However, non-convulsive seizure (NCSzs) semilogy is pleomorphic and too subtle clinically to be noticed by clinicians. Most often, mental status impairment is the presenting feature. EEG provides insight into the thalamocortical function in patients with impaired consciousness. Continuous EEG (cEEG) monitoring allows the detection of changes in the function of this system at a reversible stage, often when there are no clinical indications of such phenomena. In addition, EEG provides reasonable spatial resolution and excellent temporal resolution. This makes cEEG an excellent method for supplementing single or serial recordings in the detection and management of NCSzs/NCSE.[3] Previous difficulties associated with the bedside use of the EEG have been largely eliminated with recent advances in digital EEG acquisition, storage, quantitative analysis, and transmission. This has made cEEG monitoring in the neurological intensive care units (NICU) technically feasible.[4]

NCSzs and NCSE – Why cEEG?

Emerging data support a higher than previously thought incidence of non-convulsive epileptic activity in critically ill patients in NICU.[2] Because of the pleomorphic clinical features that can be seen with NCSzs and NCSE, cEEG is the diagnostic cornerstone, and electro-clinical correlation allows rapid diagnosis and management.

NCSzs are not uncommon in critically ill patients in NICU and were recorded in 34% of patients undergoing cEEG in NICU[5] and in 37% of comatose patients without signs of seizure activity.[6] In the Columbia study seizures were detected in 19% of patients who had cEEG monitoring; the seizures were exclusively NCSzs in 92% of patients.[7]

The reported incidence of NCSE in critically ill neurological patients was quite variable and probably related to the

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patient population studied. In Richmond, Virginia NCSE represented approximately 5% of status epilepticus (SE) cases.[8] In hospital series NCSE constituted approximately 20 to 23% of SE cases,[9,10] NCSE persisted in 14% of patients after controlling convulsive SE.[11] In VA Cooperative Study,[12] 20% of those with convulsive SE treated successfully clinically, still had electrographic seizures. NCSE was diagnosed in about 8% of all comatose patients without signs of seizure activity.[13] In a group of selected NICU patients, 23 (47%) of 49 patients with NCSzs were in NCSE.[14] In the Columbia study NCSE accounted for 59% of NCSzs.[7] There is hardly any reported data on NCSE from India. In our NICU in the last two years we could identify 22 patients with NCSE and in 50% of them NCSE was identified by cEEG monitoring (unpublished data).

cEEG - Technical Note

Recent advances in digital EEG have made cEEG monitoring in the NICU technically feasible. With digital EEG monitoring, post hoc filtering, re-montaging, adjusting of the sensitivity, and off-site reading of the EEG record are possible. cEEG is recorded digitally to storage media with standard or small-footpoint EEG recording devices. For most NICU applications, recording rates of 128-256 samples/s/channel provide adequate resolution for reliable interpretation.[4] The recording is done using 21 electrodes placed according to the International 10-20 System. In view of the high level of 60-Hz background activity in the ICU, it is advisable to record or at least display EEG with a 60-Hz notch filter in place. Recording synchronized video with EEG is essential for maximizing the efficiency and accuracy of cEEG interpretation. The role of the EEG technologist is particularly important in these patients to aid in recognizing and minimizing artifact, to enhance communication between electroencephalographers and clinicians, to assess the effect of alerting stimuli, and to note possible subtle clinical correlates of electrographic seizures. Some centers use quantitative EEG (QEEG) tools such as compressed spectral array (CSA). Use of CSA can allow visualization of prolonged trends that are difficult to appreciate on raw EEG. CSA data helps in assessing the progression of the cause of NCSE.

The problems associated with long-term EEG recordings in the NICU include: (1) faulty electrodes, either single- or multiple-scalp electrodes or ground or reference electrodes; (2) connections of electronic equipment; (3) induced artifacts from electronic devices and non-electronic equipment; (4) electrode placement issues; and (5) biological, including movement-related, artifacts. Continuous quality improvement strategies should be implemented to minimize problems. Prompt troubleshooting and regular review sessions are two important components.[15] Maintaining patient-to-EEG interface in obtunded or comatose patients is a major problem. The various approaches practiced include subdural needle electrodes glued to the scalp with collodion, subdural needles stapled to the scalp with surgical staples, and standard disk electrodes glued to the scalp with collodion.[4]

There is no consensus on the time duration of recording to record NCSE electro-clinical correlation. The diagnosis of NCSE is dependent on demonstrating the presence of ongoing seizure activity without convulsive movements. For the diagnosis of NCSE these EEG-ictal episodes should be continuous or recurrent for >30 min without improvement in clinical state or return to preictal EEG pattern between seizures.[1] At times this may require prolonged monitoring. Available evidence suggests that at least 24 hours recording is essential. Seizures were detected within the first 24 hours of cEEG monitoring in 88% of all patients who would eventually have seizures detected by cEEG. In another 5% the first seizure was recorded on monitoring day 2, and in 7% the first seizure was detected after 48 hours of monitoring. Comatose patients were more likely to have their first seizure recorded after >24 hours of monitoring.[7]

NCSE - Diagnosis

In a given clinical setting it is the cognitive or behavioral change from the patient's baseline (which may be abnormal) that would suggest the possibility of NCSE. However, in patients with mental retardation, encephalopathy, or major psychiatric disease there may be difficulty in identifying what constitutes a change in the baseline status. The lethargy or drowsiness seen in these contexts may mask a non-convulsive state. Diagnosis of NCSE involves the clinical picture of an abnormal mental status with diminished responsiveness, a supportive EEG, and often responsiveness to benzodiazepine administration. The diagnosis may be difficult in two situations. First, if the patient is comatose and has another reason for encephalopathy, then even if seizure activity stops, coma may continue so a clinical response to benzodiazepines is not a reliable indicator. Secondly, the EEG pattern may not be highly rhythmic or epileptiform. If there is an equivocal response to benzodiazepines in the latter case, then the diagnosis cannot be established entirely from the EEG and other clinical factors must be used to establish the diagnosis.[1]

An emerging unifying hypothesis of NCSE has been to divide NCSE based on presence of a primary epileptic encephalopathy in which mental status changes are due to seizure activity or electrographic NCSE in which the electrographic pattern of NCSE is present but encephalopathy is most likely due to some other brain insult.[2] Kaplan[1] developed a more detailed classification utilizing clinical characteristics to categorize patients, especially mental status (1) localization-related NCSE, (2) generalized NCSE (GNSE), and (3) indeterminate or intermediate NCSE. GNSE is further divided into: (1) Absence status epilepticus (ASE) associated with

childhood absences or rarely with juvenile myoclonic epilepsy (JME), (2) patients with childhood onset, secondary generalized epilepsy, often with mental retardation, often with greater confusion and myoclonus; (3) elderly patients without epilepsy who present de novo, usually with toxic or metabolic dysfunction, intake of psychotropic drugs or benzodiazepine withdrawal, and (4) generalized non-convulsive status secondary to partial epileptic status of temporal or frontal lobe origin. Recently, Shneker and Fountain[16] categorized patients based on the easily observable characteristics of etiology, mental status, and presence of complications, thus relying less on the interpretation necessary for traditional classification. Such an approach helps the clinician to predict the probable outcome in a particular clinical setting and also to decide the appropriate therapeutic options.

Electrographic Seizures or NCSzs - Diagnostic EEG Criteria

Young et al[17] proposed primary and secondary criteria for an electrographic seizure or a NCSz (Table 1). To qualify, at least one of the primary criteria and one or more of the secondary criteria, with discharges of >10 sec are required. For the diagnosis of NSCE these EEG-ictal episodes should be continuous or recurrent for >30 min without improvement in clinical state or return to preictal EEG pattern between seizures.

Litt et al[18] defined electrographic seizures as distinct discharges that evolve over time with a change in the frequency, amplitude, and distribution and described three EEG patterns of electrographic SE: focal, (Figure 1) generalized, and bihemispheric. With these criteria it is relatively easy to diagnose NCSE when there are frequent electrographic seizures, particularly when they are focal. However, with regard to generalized discharges, there are serious limitations, as the authors did not include invariant spike-and-wave discharges; there was usually a waxing and waning of these patterns for inclusion. This can often be a very subjective interpretation.

Table 1: Criteria for an electrographic seizure or a non-convulsive seizure proposed by Young et al[17]

Primary criteria
1. Repetitive generalized or focal spikes, sharp waves, spike-wave and wave, or sharp-and-slow wave complexes at more than three per seconds
2. Repetitive generalized or focal spikes, sharp waves, spike-and-wave, or sharp-and-slow wave complexes at fewer than three per second and secondary criterion # 4
3. Sequential rhythmic waves and secondary criteria 1, 2, and 3 with or without 4

Secondary criteria
1. Incrementing onset: increase in voltage and/or increase or slowing of frequency
2. Decrementing offset: decrease in voltage or frequency
3. Post-discharge slowing or voltage attenuation
4. Significant improvement in clinical state or baseline EEG after intravenous antiepileptic drug

To qualify at least one of the primary criteria 1-3 and one or more of the secondary criteria, with discharges ≥ 10 seconds.

NCSzs - EEG Characteristics

EEG characteristics of NCSzs/NCSE are heterogeneous. Morphology is highly variable and includes typical spike-wave (TSW) discharges, atypical spike-wave (ATSW) (Figure 2 and 3) multiple or polyspike wave discharges (MSW) (Figure 4), and rhythmic delta activity with intermixed spikes (RDIS) (Table 2). The morphology of the ictal discharges may vary during the course of a single EEG. Discharge frequency may be between 1 to 3.5 Hz and only a small proportion (4%) may have 3 Hz or faster frequencies.[16,18,19] NCSE can be classified on EEG grounds as generalized, focal, or generalized with a focal emphasis.[19]

Periodic epileptiform discharges (PED), periodic lateralized epileptiform discharges (PLED), generalized PED (GPED), bilateral independent PLED (BiPLED), triphasic waves, frontal intermittent rhythmic delta activity, and suppression-burst activity are frequently seen in patients with seizures on cEEG

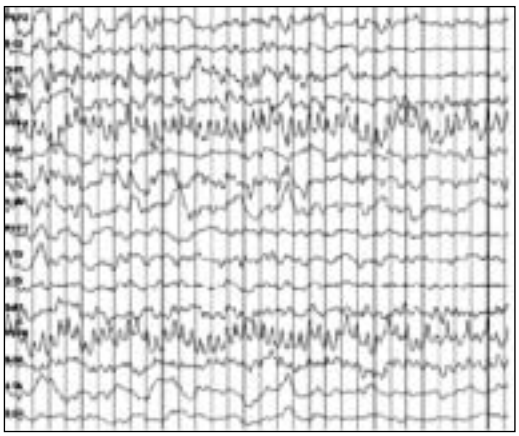

Figure 1: EEG showing focal right frontal ictal discharges in a patient with localization-related nonconvulsive status epilepticus

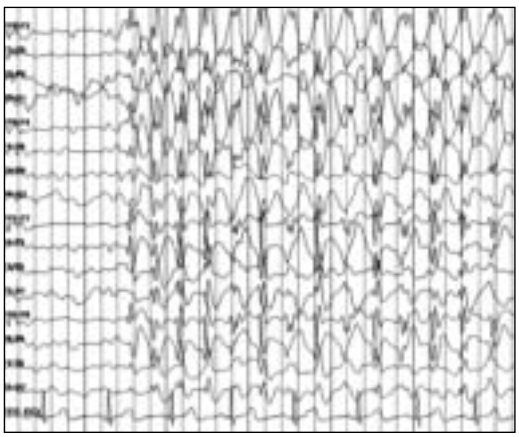

Figure 2: EEG showing generalized typical 3Hz spike-wave activity in a patient with generalized nonconvulsive status epilepticus – Absence status epilepticus

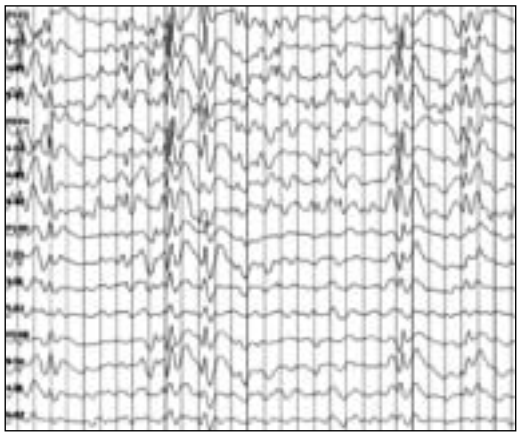

Figure 3: EEG showing generalized atypical spike-wave discharges in a patient with generalized nonconvulsive status epilepticus

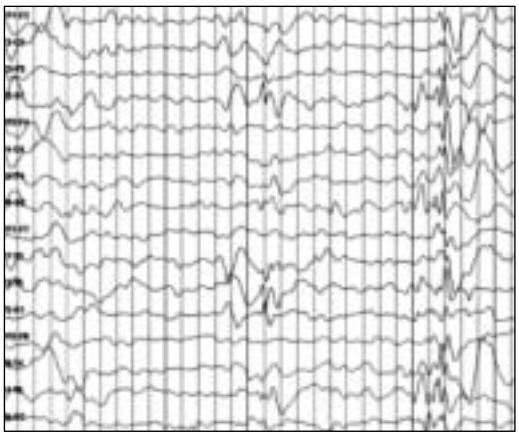

Figure 4. EEG showing multifocal and polyspike-wave discharges in a patient with nonconvulsive status epilepticus – Both localization related and generalized

Table 2: EEG discharges – Morphological classification*

Typical spike and wave (TSW)	3–3.5 Hz spike-wave and slow-wave complexes that are generalized from onset, synchronous and symmetric
Atypical spike and wave (ASW)	Spike- and slow-wave complexes that lack one or more of the features of TSW (e.g., frequency < 3Hz or asymmetric appearance)
Multiple spike and wave	Repetitive complexes of two or more spikes followed by a (MSW) slow wave
Rhythmic delta with Intermittent spike (RDIS)	High amplitude, repetitive, rhythmic, focal or generalized delta activity with intermittent spikes or sharp waves
Periodic epileptiform discharges	Repetitive sharp waves, spikes, or sharply contoured waves at regular or nearly regular intervals and without (PED) clear evolution in frequency or location.
Periodic lateralized Epileptiform discharges (PLED)	Consistently lateralized PED
Generalized PED (GPED)	Bilateral and synchronous PED with no consistent lateralization
Bilateral PLED	PLED occurring bilaterally, but independently and (BiPLED) asynchronously
Triphasic waves	Generalized periodic sharp waves or sharply contoured delta waves with triphasic morphology at 1-3 Hz, with/without anterior-posterior or posterior-anterior lag
Frontal intermittent (FIRDA)	Moderate- to high-voltage monorhythmic and sinusoidal 1- rhythmic delta 3-Hz activity seen bilaterally maximal in anterior leads, activity no evolution

Source: Ref: 7,17

monitoring (Table 2). However, many of these are controversial, particularly as to whether they are ictal.[7,20] PLEDs are seen frequently in the aftermath of SE[21,22] and have been associated with poor outcome.[23,24]

The frequency of various ictal discharges was variable in different studies. In the series by Granner and Lee[19] ictal discharges were generalized (TSW: 7%; ASW; 53%; MSW: 20%; RDIS: 20%) in 69%, diffuse with focal (ASW: 53%; RDIS: 47%) predominance in 18%, and focal (ASW: 64%; MSW: 9%; RDIS: 27%) in 11%. In this study the morphologies and patterns and persistence varied greatly. Young et al[17] reported repetitive focal spikes or sharp waves showing variable spread in 57%; generalized polyspikes or polyspike-wave with focal onset or accentuation in 16%, generalized sharp waves or generalized sharp- or slow-waves complexes < 3 Hz in 10%, focal rhythmic waves with intermittent spikes in 8%, lateralized spikes or sharp waves in 4%, rhythmic waves of varying amplitude and frequency in 2%, and generalized polyspikes and waves in 2% patients. In another study the discharges were generalized in 59% and lateralized or localized in 41%.[16] Thus the EEGs in a wide variety of cases of NCSE share three typical features: (1) epileptiform spike or sharp wave discharges or very rhythmic slowing with sharp features; (2) rhythmicity; and (3) recurrence frequencies of > 1 Hz.

Certain EEG patterns are more commonly associated with the underlying etiology. Spike-wave (whether or not general-

ized) and generalized EEG discharges were much more likely to be seen in the epilepsy group than in patients with NCSE due to acute medical illness.[16]

cEEG Monitoring – When?

Available evidence indicates that NCSzs and NCSE probably occur in a substantial fraction of obtunded or unresponsive patients, 11-56% in NICU settings.[4,7,25] In a recent hospital-based retrospective study of cEEG, electrographic seizures were associated with coma; age <18 years, a history of epilepsy, and convulsive seizures during the current illness prior to monitoring.[7] In the same study, of the 105 patients with unexplained decrease in the level of consciousness as the primary diagnosis, NCSzs were recorded in 16 (16%), 5 (31%) of them had NCSE.

Electrographic seizures may persist after convulsive SE. Of the 180 patients who were monitored after clinical status epilepticus, 96 had ictal discharges, which included both NCSzs and NCSE.[23] In another study cEEG monitoring demonstrated electrographic seizures in 48% of patients and 14% manifested NCSE.[11] The present evidence suggests that electrographic burst suppression is superior to the control of clinical and electrographic seizures activity.[26]

cEEG monitoring detected NCSz/NCSE in 28% of patients with intracerebral hemorrhage (ICH) and in 6% of patients with ischemic stroke. In patients with ICH, cEEG detected four times as many electrographic seizures as occurred clinically and seizures were associated with progressive midline shift and also worsening neurological function.[27] cEEG monitoring detected NCSE for 8% of patients with subarachnoid hemorrhage and otherwise unexplained coma or neurological deterioration. The seizures were highly refractory to therapy, and the prognosis for these patients was extremely poor.[28]

Use of cEEG in patients with traumatic brain injury demonstrated that convulsive and non-convulsive seizures occured in 22% of patients, with six of them displaying SE. In more than half of the patients (52%) the seizures were non-convulsive and were diagnosed on the basis of EEG studies alone.[29]

Based on the above data the possible clinical settings for cEEG to detect NCSE can be the following:

- Patient with impaired consciousness due to acute brain injury due to any cause
- Patients with unexplained impaired consciousness
- Patients with convulsive SE not awake following treatment
- Patients with refractory SE

Diagnosis of NCSE – The Impact

The potential impact of early diagnosis of NCSE will be on the treatment and the outcomes. Duration of ictal activity and the time delay to diagnosis are independent predictors of outcome. When the NCSE duration was less than 10 hours, 60% of patients returned home and 10% died, whereas when the NCSE duration was more than 20 hours none returned and 85% died. This was independent of etiology. With regard to delayed diagnosis, when the NCSE was diagnosed in less than 30 minutes, 36% died and when the NCSE was diagnosed after more than 24 hours, 75% died.[16]

Mortalities were higher in acute symptomatic NCSE (27%) vs. the epilepsy-related (3%) and cryptogenic NCSE (18%). Similarly, mortalities were higher in patients with severe mental status impairment (39%) when compared to those with mild impairment (7%).[19] This data from cEEG monitoring with regard to NCSE has an impact on treatment strategies. Patients with epilepsy as the only cause of NCSE should probably not be routinely treated very aggressively. The rationale is that they are unlikely to die from NCSE. Patients with NCSE of cryptogenic etiologies should be treated aggressively. If NCSE is due to an acute medical illness, treatment should be aggressive and pentobarbital, propofol, or midazolam are the drugs of choice. Electrographic seizures and occasional short-lasting NCSzs may not require any specific treatment. However, it is our policy to treat NCSz clusters.

In conclusion, NCSzs/NCSE probably occur in a substantial fraction of obtunded or unresponsive patients. NCSz semiology is too subtle clinically to be noticed. Most often, mental status impairment is the presenting feature. Duration of ictal activity and the time delay to diagnosis are independent predictors of outcome. cEEG monitoring allows the detection of changes in the function of the thalamocortical system at a reversible stage, often when there are no clinical indications of such phenomena. This makes cEEG an excellent method for supplementing single or serial recordings in the detection and management of NCSzs/NCSE.

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