Table 1: Causes of non-conuvlsive status epilepticus

Causes of non-conuvlsive status epilepticus
• Head trauma
• Cerebrovascular accident
• Ischemic stroke
• Venous stroke
• Intracerebral hemorrhage
• Subarachnoid hemorrhage
• Encephalitis
• Infectious: Viral: HSV, HIV, Neurosyphilis
• Autoimmune
• Paraneoplastic
• Slow viral: CJD
• Medications
• Overdose
• Antibiotics: Cephalosporins, Penicillins, Quinolones, Imipenem
• Methotrexate, Tiagabine, Lithium, Pseudoephedrine, Tramadol, Chloroquine, Ifosfamide, Baclofen, Cyclosporine
• Withdrawal
• Benzodiazepines, Opioids, Baclofen
• Genetic/developmental (PREVIOUS EPILEPSY)
• Mitochondrial disorders: MELAs,
• Lafora body disease
• Lennox Gastaut syndrome
• Ring chromosome 20
• Cortical dysplasia

to as subtle NCSE.[20] Subtle NCSE is common, but the diagnosis may be delayed or missed because the altered level of consciousness can mimic postictal encephalopathy or delirium,[52] leading to increased mortality.[14]

NCSE in critical illness

CEEG recordings of adults in the ICU estimate the overall rate of NCSE at about 10–20%[53] and this increases to about 30% in critically ill patients[18] this includes patients with acute brain injuries, but it is rarely the admission diagnosis, as patients develop NCSE after the inception of the critical illness.[54]

Traumatic brain injury

About 10% of patients with TBI have NCS based on CEEG recordings,[55,56] and these are linked to elevated intracranial pressure and cerebral metabolic distress, that may t lead to additional brain damage[57,58] and worse outcome.[59]

Cerebrovascular insult

Ischemic stroke

NCS are more common than convulsive seizures in the 9% of patients who have seizures after an acute ischemic stroke.[60,61] Ischemic stroke constitutes 20% of all causes of NCSE among comatose patients in the ICU[17] and about 18% of patients with intracerebral hemorrhage have NCSE on CEEG.[62,63]

Subarachnoid hemorrhage

NCS and NCSE were diagnosed in 7–18% of patients of SAH,[53,54,64,65] and was associated with older age and higher mortality. NCSE beyond the 5th day after SAH was associated with 100 % mortality,[64] supporting the need for rigorous treatment of NCSE that follows SAH. However the role of prophylactic AEDs is unclear.[65]

Encephalitis

Both infectious and noninfectious causes of encephalitis are well established causes of SE including NCSE, with seizures (often non convulsive) being associated with autoimmune encephalitis in 78% of patients.[66] Autoimmune and paraneoplastic encephalitis accounted for 40% of a case series of new onset refractory SE,[67] but systematic data on the incidence of NCS and NCSE in encephalitis is lacking.

Hypoxic ischemic encephalopathy

NCS and SE, occurs in up to 30% of patients who remain comatose after surviving cardiorespiratory arrest (CRA).[68] In most of these patients, the brain injury is severe and largely irreversible and usually associated with extremely poor outcomes, independent of the NCSE[69] and it is unclear whether treatment with AEDs improves the catastrophic prognosis.[70,71]

Favorable outcomes may be expected in a small subgroup (viz age <65 years, conversion to a shockable rhythm and prehospital return of spontaneous circulation during resuscitation.[72] Reactive pupils and motor reflexes and 3 days after CRA[73] and a reactive EEG background significantly improve prognosis.[74-76]

The epileptic nature of postanoxic myoclonus is still a matter of debate.[77] Acute post hypoxic myoclonus may have cortical or subcortical mechanisms[78], but early post anoxic myoclonus within 24 h is a predictor of poor outcome,[79] Cchronic post hypoxic myoclonus on the other hand is often stimulus sensitive and has a lear cortical basis.[80]

Medications and drugs

A variety of drugs including a range of antibiotics[81] have been implicated for an increased seizure risk, especially with underlying renal dysfunction, brain lesions or epilepsy. Antiepileptic drugs such as tiagabine and an overdose of carbamazepine or lamotrigine may also trigger ASE.[38] Other drugs have been implicated include baclofen, opioids and its antagonists, anticancer drugs, methotrexate as well as withdrawal of antiseizure medications such as benzodiazepines [Table 1].

DIAGNOSIS OF NCSE

NCSE can manifest with a number of different symptoms, altered mental status being the most common, occurring in 82% of patients. Among these, the specific manifestation was confusion in 49%, coma in 22%, lethargy in 21%, and memory loss in 8%.[82] A rapid and unexpected emergence of any of these symptoms in the absence of another plausible explanation should raise a suspicion of NCSE. On the other hand, a number of conditions may resemble NCSE

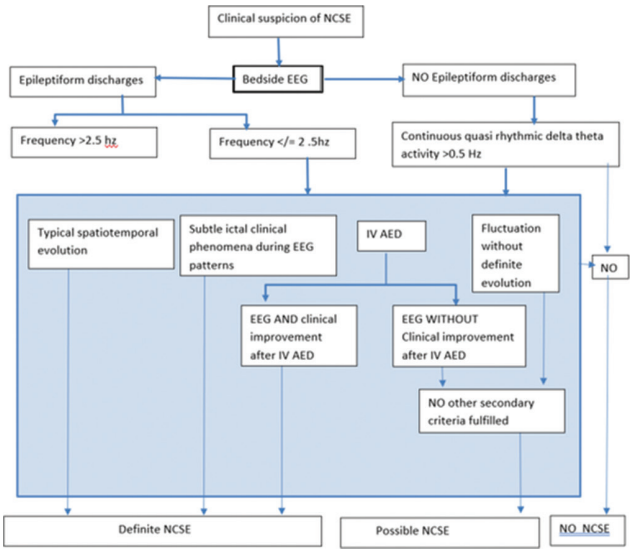

Figure 1: Salzburg EEG criteria for NCSE. NCSE: Non-convulsive status epilepticus, EEG: Electroencephalogram. (Adapted from Leitinger *et al*. Lancet Neurology 2016;15:1054-62)

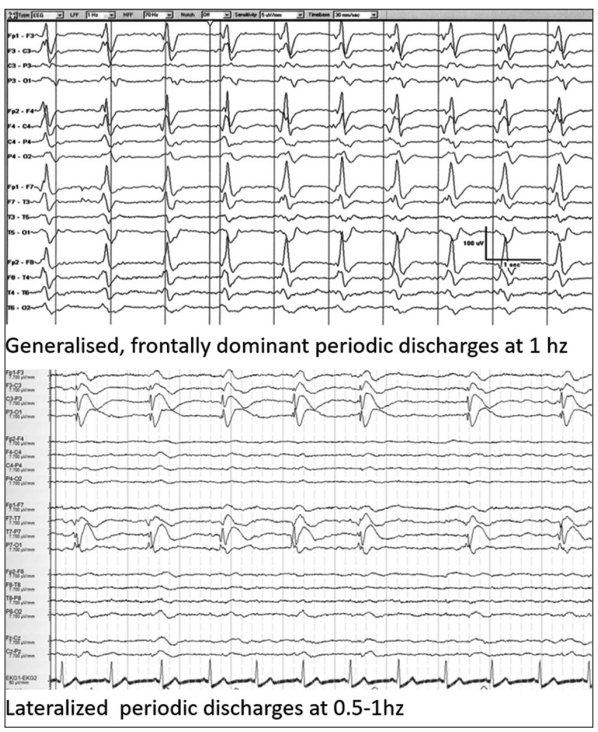

Figure 2: Ambiguous EEG patterns: The ictal interictal continnum. EEG Patterns in these two figures will need further evaluation for fluctuations in frequency and morphology, clinical correlations and response to IV benzodiazepine before establishing a diagnosis of non convulsive status epilepticus. Refer to Salzburg EEG criteria (Benickzy S 2013)

a purely clinical diagnostic test when EEG is unavailable [Box 2]. While this is useful in "proper NCSE," its value in other generalized periodic patterns such as triphasic waves of hepatic encephalopathy, Creutzfeld Jakob Disease and Epileptic encephalopathies, where the EEG may improve without corresponding improvement in the clinical behavior Johnson *et al*. 2017,[102] Gelisse *et al*. 2019[103] is questionable. Moreover, many of these patterns disappear spontaneously in sleep.

EEG in coma after HIE

Especially in patients with severe cerebral hypoxia, a particularly confusing scenario is the presence clinical myoclonus in the first few days with EEG burst suppression patterns of various degrees that mimic NCSE., available data do not indicate that pharmacological treatment of either the EEG alterations or early posthypoxic myoclonus has any positive impact on the patient's prognosis.[17,79] Administration of anticonvulsants in such cases appears to be just EEG cosmetics.[94] It important to note that while less myoclonus may be relief for nurses and family members, the comatose patient himself does not have any benefit from such treatment.

On the other hand, EEG can provide prognostic information in hypoxic–ischemic encephalopathy after CRA.[104] Seizures are detected in up to 40% of CRA survivors in a coma, and have been associated with adverse outcomes.[105,106] EEG patterns, such as burst-suppression, nonreactive background activity, or isoelectric EEG recordings are indicators of an unfavourable prognosis.[107] Although prognostication of poor outcome seems reliable, predictions for good prognosis still remain inaccurate.[105]

Imaging in NCSE

Imaging is mandatory when investigating focal SE, particularly at first presentation, to exclude a structural cause. Often there is a higher likelihood of identifying a remote symptomatic cause. On the other hand, patients with absence SE would be expected to have normal conventional neuroimaging. Transient changes on DWI and T2-FLAIR sequences are seen in up to half the patient with SE.[108] However, signal changes in the cortex may be falsely localising and may also involve the thalamus and pulvinar ipsilateral to the epileptiform activity. Leptomeningeal enhancement, luxury perfusion on MR angiography and diminished focal cortical veins on susceptibility weighted imaging may be noted in hyperperfused ictal regions.[109,110] Arterial Spin Labeling shows high CBF in the cortical epileptogenic zone, the ipsilateral pulvinar, and the contralateral cerebellum. A major challenge with these MRI findings is that we do not know how long the signal change persists after the cessation of SE: perfusion normalizes from seconds to minutes after the end of the episode, whereas signal changes on DWI and T2/FLAIR may require up to several weeks to resolve.[108]

Functional imaging studies such as the PET and SPECT may show abnormalities which indicate an unstable neuronal metabolic situation. This may, at best, support the diagnosis

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