

Transient loss of consciousness

Rachael Power, Neurology ST7





Making a diagnosis

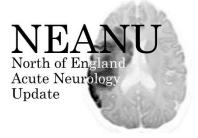


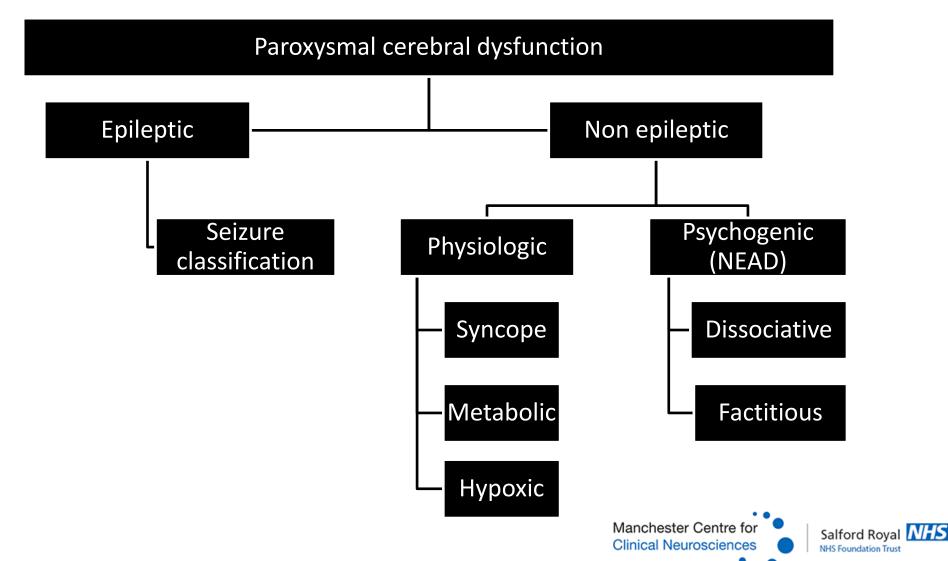
- To make a diagnosis in blackouts
 - Reconstruct the event from descriptions (collateral from eyewitness). Before, during,
 after.
 - Obtain video
 - Video EEG
- 12 lead ECG in all patients
- Judicious use of imaging and EEG
- Discussion with neurology / epilepsy service
- First seizure clinics
- Discussion around driving / employment

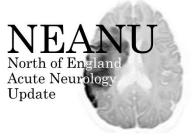
'a routine inter-ictal EEG is one of the most abused investigations in clinical medicine and is unquestionably responsible for great human suffering'

Chadwick D. Diagnosis of epilepsy. Lancet. 1990;336:291–5



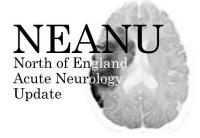


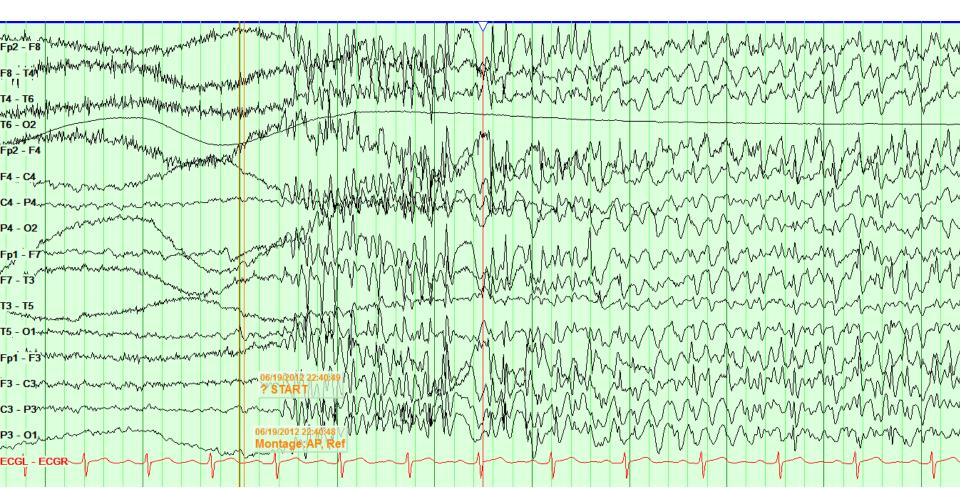




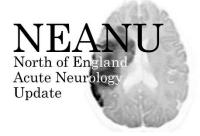
What is the nature of the attack?

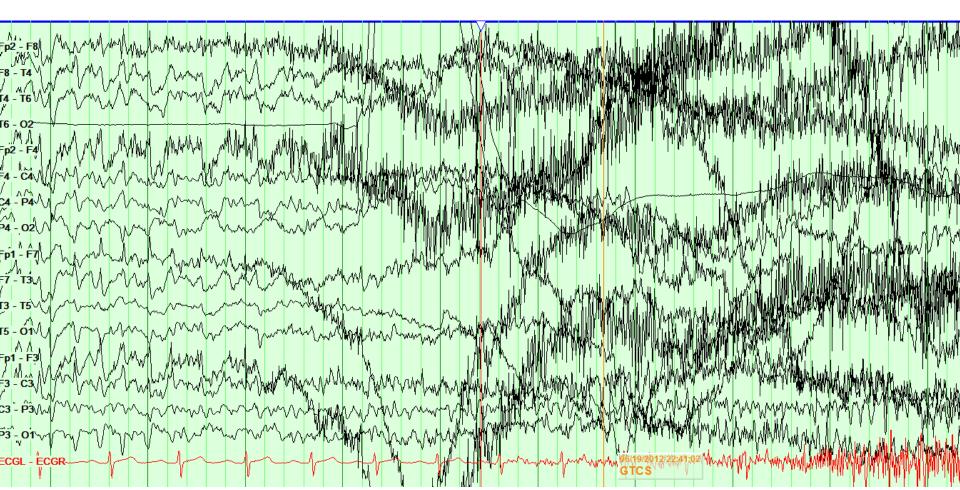






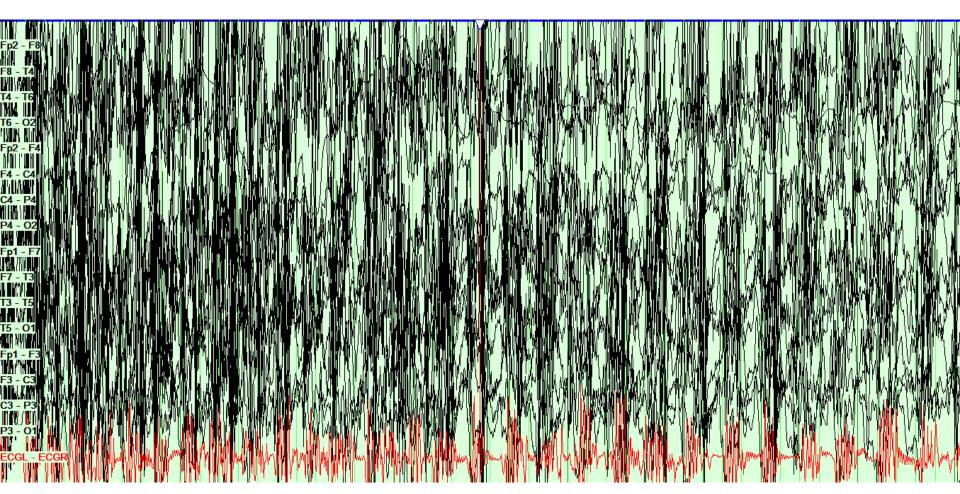






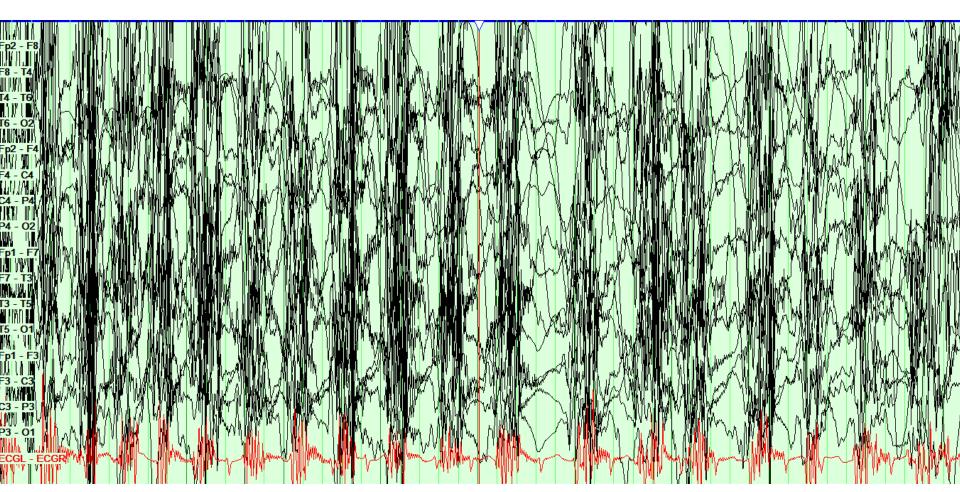




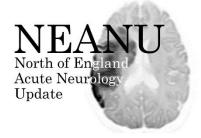


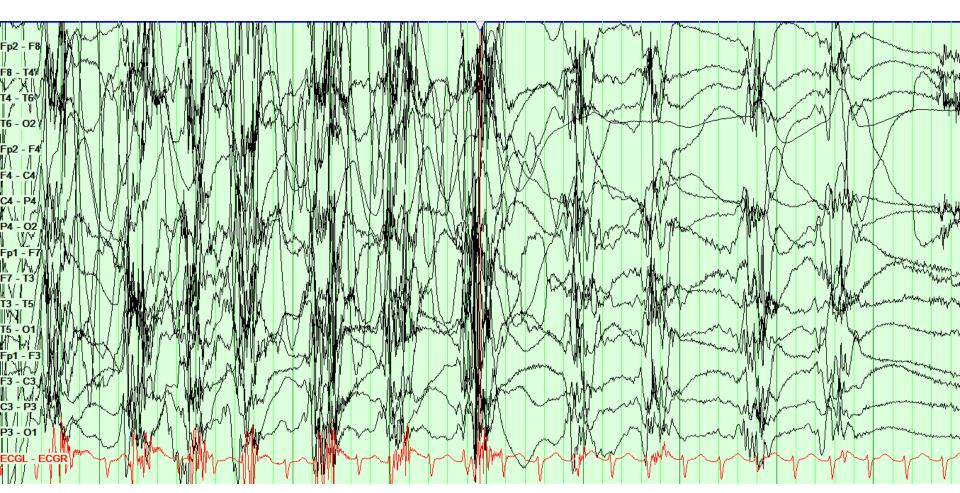








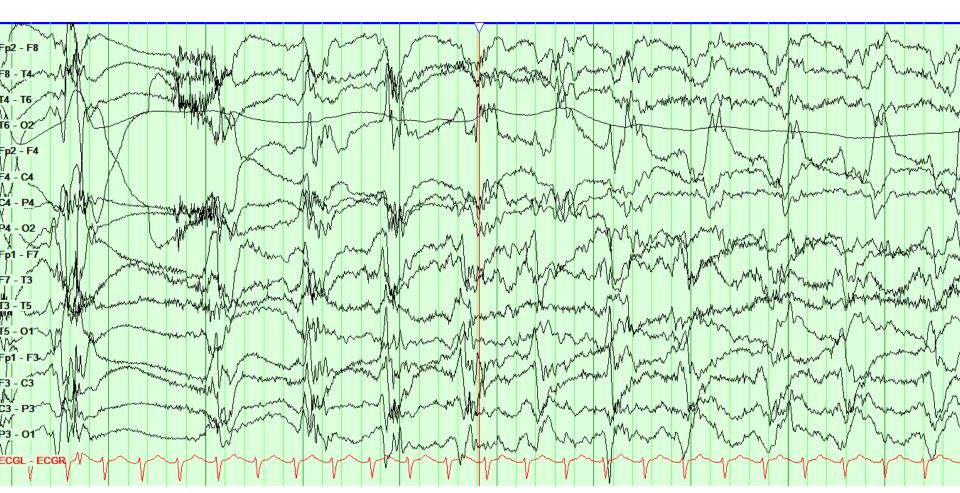




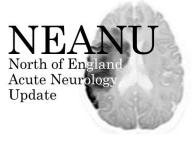












What is the nature of the attack?

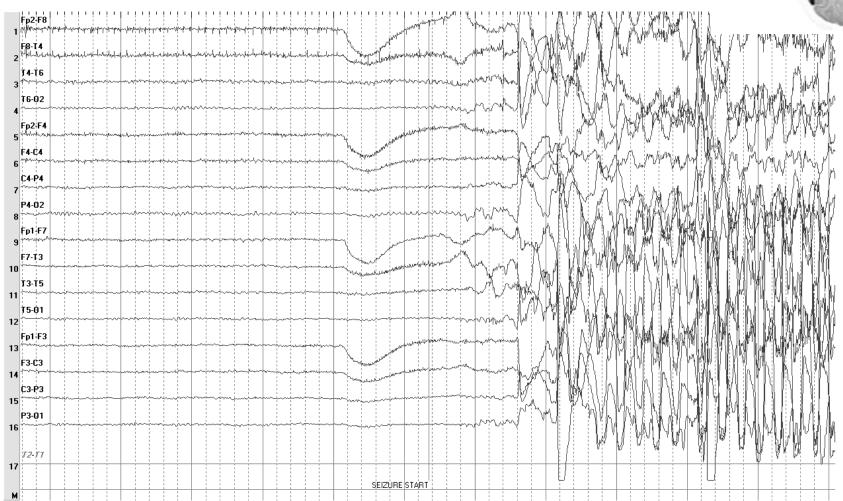






EEG during dissociative event





A sudden onset of completely obscured EEG with a mixture of movement and muscle artefact.

















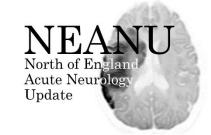
Abrupt termination of convulsive episode. When the artefact disappears there is no postictal slowing or suppression, there is normal alpha rhythm.







Non epileptic attack disorder (NEAD) Psychogenic non epileptic seizures (PNES) Dissociative attacks



- High frequency of events
- Prolonged events (A significant proportion of apparent 'status' in inpatients)
- Attacks in medical situations (waiting room, scanner)
- History of other unexplained medical conditions
- Very gradual onset or termination

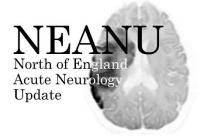


- Discontinuous (stop-and-go)
- Irregular, or asynchronous (out-of- phase) activity including side-to-side head movement
- Pelvic thrusting and opisthotonic posturing
- Post-ictal crying





Semiology of Non epileptic attacks



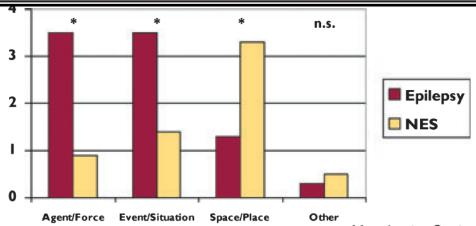
- Six different types of PNES:
 - Rhythmic motor tremor or rigor-like movements 46.7%
 - Subjective sensations 23.6%
 - Unresponsiveness without motor manifestations 11.2%
 - Complex movements (eg:back arching/pelvic thrusting)- 10%
 - Hypermotor PNES (violent movements) 3.3%
 - Mixed 5.2%
- Stereotyped in 82% of cases.



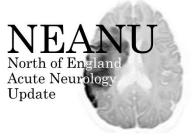
It's how they say it...



Table 2. Examples of metaphor types in the three most common conceptual categories					
Category	Seizure as an agent/force	Seizure as an event/situation	Seizure as a space/place	Other	
Grammatical subject	Sei zure	Seizure	Patient	Variable	
Semantic agency	With the seizure	Variable	With the patient	Variable	
Examples	Seizures come, go, come in, come on, come up, creep up on you, get you, try to do things, set off, are sent in, are straight there, are fought, counteracted, contained, are let pass, wear off	Seizures happen, occur, take place, are due, start, finish, go on, carry on, develop, are experienced, witnessed, handled, controlled, stopped, avoided/put off, are brought on, run their course	Drifting off, being off somewhere else, going, going off, being gone, coming back, coming round, coming to, going down, being down, not being there, being out into seizures, in seizures, out of seizures, within seizures, through seizures	Seizures are started up, are fixed, like an electrical charge, like the lights are on but nobody's at home, like something going off, like shutting a computer off, like cold or hot water on the top of your head, are as if your head carries on without you	







What is the nature of the attack?



Motor activity associated with syncope



Lempert T, Bauer M, Schmidt D. Syncope: a videometric analysis of 56 episodes of transient cerebral hypoxia Ann Neurol. 1994; 36: 233-237

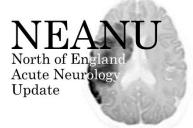


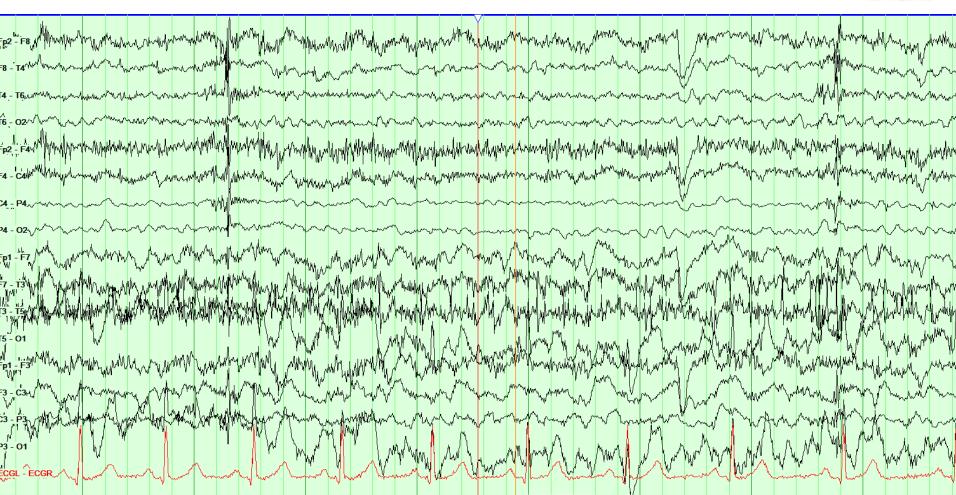
Syncope



- Some motor activity is common
 - Multifocal twitching
 - Occasionally stiffening
- More pronounced in
 - Prolonged (not recumbent)
 - Severe (cardiogenic)
- Distinguishing from GTCS
 - Typical prodrome in vasovagal syncope
 - Brevity
 - Lack of post ictal features



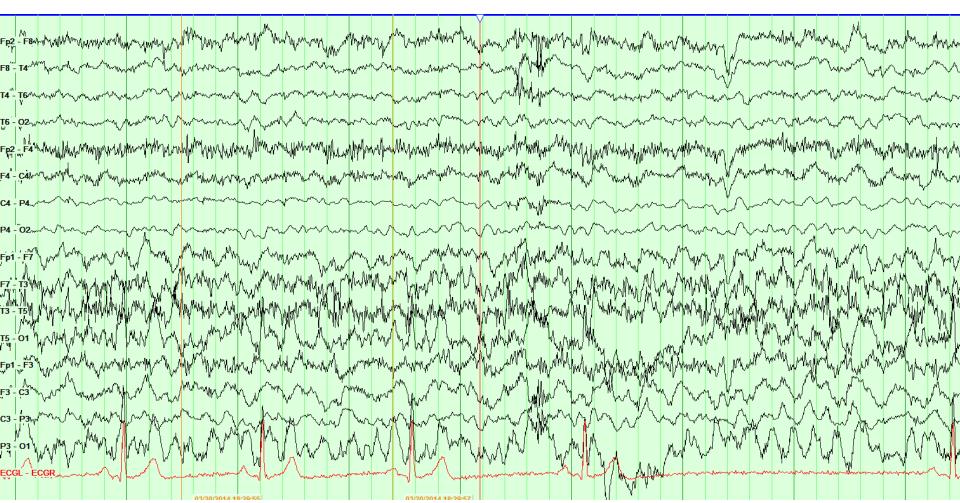






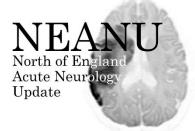


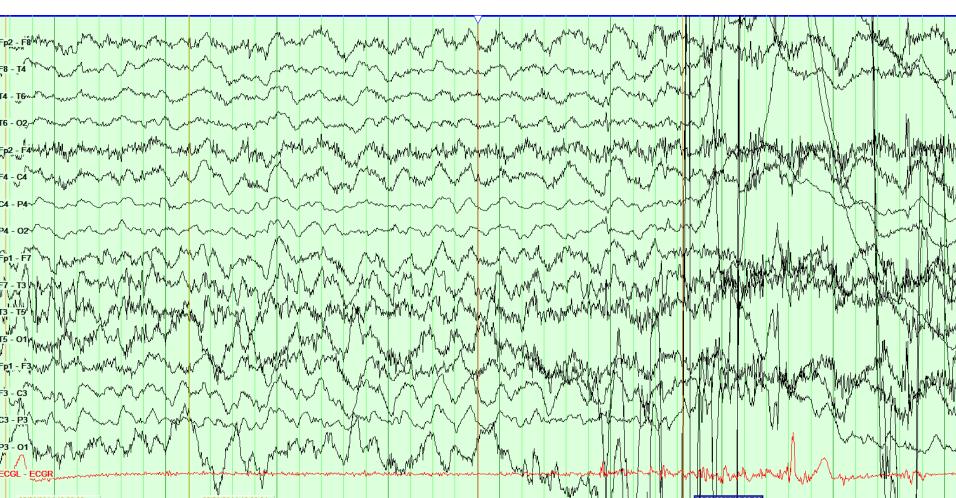








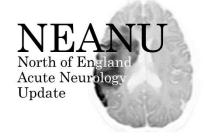






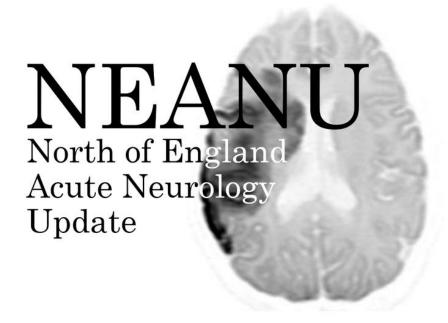


Conclusion



- To make a diagnosis in blackouts
 - Reconstruct the event from descriptions
 - Obtain video*
 - Video EEG
- Non epileptic attacks are very common among inpatients
- Metabolic disorder frequently cause blackouts in acute medical settings

Manchester Centre for Clinical Neurosciences Salford Royal NHS Foundation Trust



Diagnosis and management of

Status epilepticus

Rajiv Mohanraj





What is status epilepticus?

"Status epilepticus occurs when a seizure persists for a sufficient length of time or is repeated frequently enough to produce a fixed or enduring epileptic condition" *Gastaut 1970*

"Generalized, convulsive status epilepticus in adults and older children (>5 years old) refers to >=5 min of continuous seizures or two or more discrete seizures between which there is incomplete recovery of consciousness"

Lowenstein et al 1999

"Status epilepticus is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms which lead to abnormally prolonged seizures (after time point t $_1$). It ...can have long-term consequences (after time point t $_2$), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures"

ILAE Task Force on Status Epilepticus, 2015

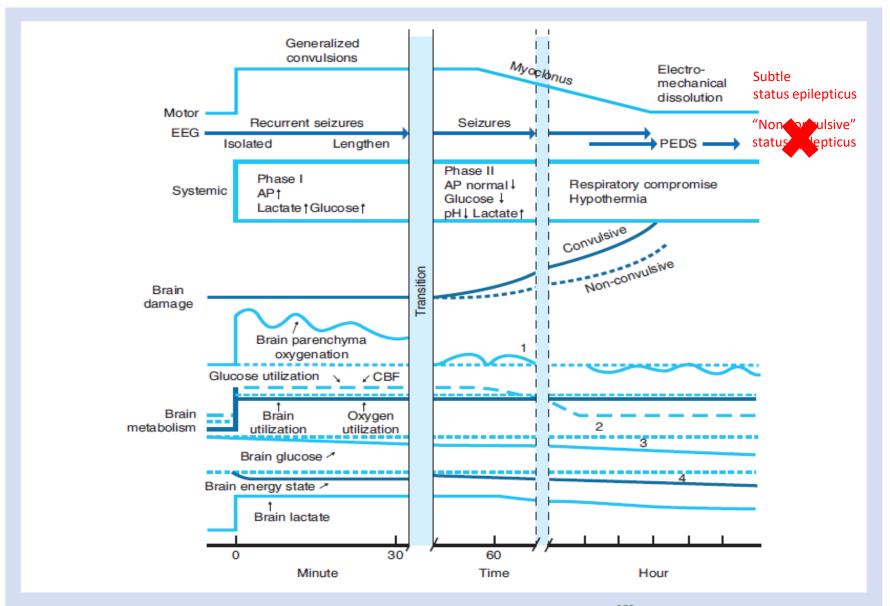


Fig 1 Physiological changes occurring during prolonged status epilepticus. Adapted from Shorvon.¹⁰⁶ PED, periodic epileptic discharge; CBF, cerebral blood flow. 1, Loss of reactivity of brain oxygen tension; 2, mismatch between the sustained increase in oxygen and glucose utilization and a decrease in cerebral blood flow; 3, a depletion of cerebral glucose and glycogen concentrations; 4, a decline in cerebral energy state.

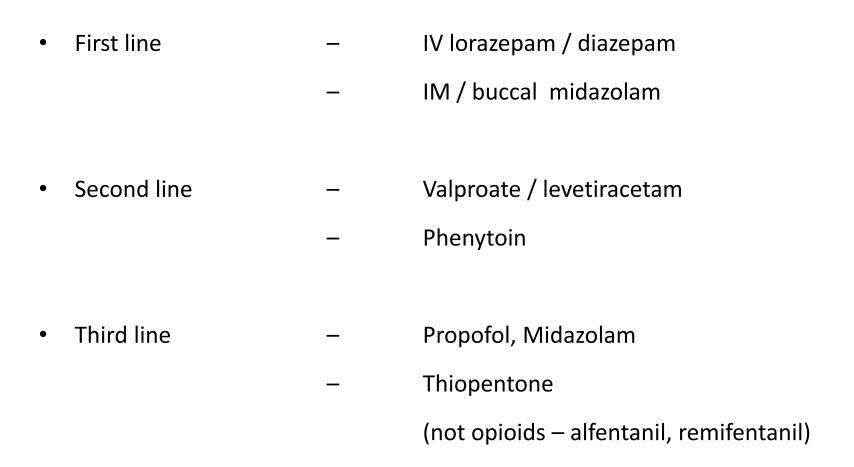
Salford Royal NHS Foundation Trust (SRF Pennine Acute Hospitals NHS Trust (PAT)



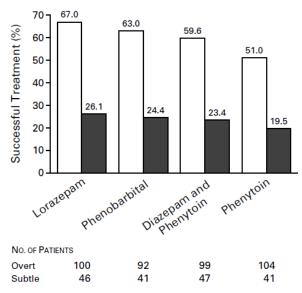
Status Epilepticus and Prolonged Seizures Guideline for Management in Adults

Lead Author:	Rajiv Mohanraj, Consultant Neurologist			
Additional author(s)	Varduhi Cahill, Consultant Neurologist			
	Matt Jones, Consultant Neurologist			
	Katherine Harwood, Neurology Specialist Pharmacist			
Division/ Department::	Neurosciences			
Applies to: (Please delete)	Salford Royal Care Organisation			
Approving Committee	Medicines Management Group			
Date approved:	16/03/2020			
Expiry date:	March 2023			

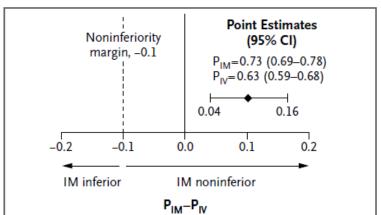
Drug treatment of convulsive status epilepticus

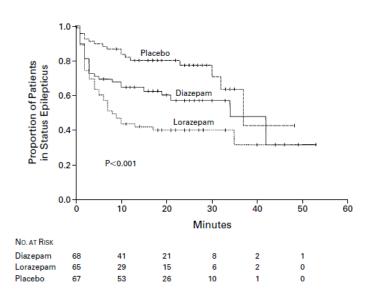


Landmark RCTs of benzodiazepines in SE

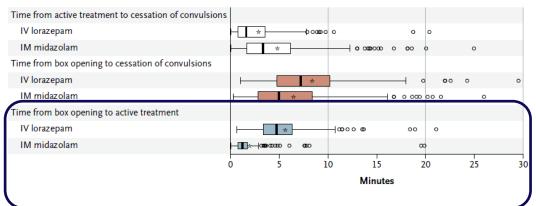


Treiman D et al. N Engl J Med 1998; 339: 792-798





Alldredge et al. N Engl J Med 2001; 345: 631-637



Silbergleit et al. N Engl J Med 2012;366:591-600



Status Epilepticus and Prolonged Seizures Guideline for Management in Adults

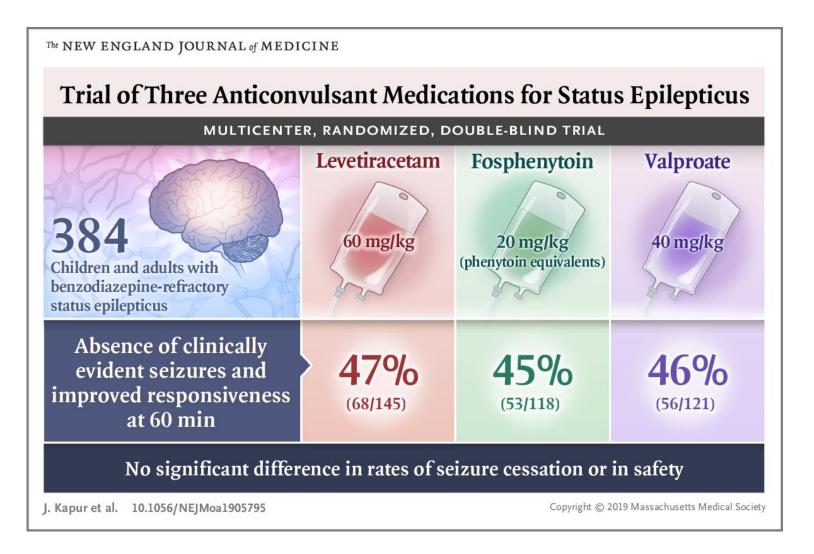
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First line treatment of convulsive SE

- Patient with IV access
 - Lorazepam 4 mg IV
 - Diazemules 10 mg IV (current shortage)
 - If unavailable, IM / IV/ buccal/ nasal midazolam 10 mg
- Patient without IV access
 - Midazolam 10 mg (buccal or IM)
 - Rectal diazepam not to be used routinely

Second line treatment

Established Status Epilepticus Treatment Trial (ESETT)



Salford Royal NHS Foundation Trust (SRFT)
Pennine Acute Hospitals NHS Trust (PAT)



Status Epilepticus and Prolonged Seizures Guideline for Management in Adults

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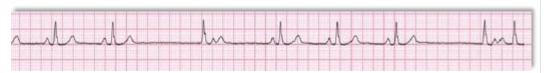
Second line treatment of convulsive status epilepticus

- IV levetiracetam 60mg /kg (max 4500mg, ≥75kg) over 10 minutes
- Maintenance dose 1.5g BD

- IV sodium valproate 40 mg/kg (max 3000 mg, ≥75kg) over 10 minutes
- Maintenance dose 600mg TDS

Phenytoin

- IV Phenytoin 20mg/kg (2g max)
- Infusion rate
 - 25-50mg/min (max 50mg/min)
 - 10-25mg/min for elderly, cardiac disease
- Serum concentration 2 hours after loading
 - Further loading if required
- Maintenance dose 100mg TDS



See appendix of SE policy for safe administration of phenytoin on wards



Classification: Official





Patient | Risk of death and severe harm from error with injectable phenytoin | 9 November 2016

Alert reference number: NHS/PSA/W/2016/010

Warning Alert

Injectable phenytoin is used to slow and stabilise erratic electrical brain activity in, for example, status epilepticus, which is a life-threatening medical emergency. Phenytoin is a particularly complicated drug to use. It is recognised as a critical medicine by UK Medicine Information (UKMI).¹

Phenytoin has a narrow therapeutic index, meaning that there is little difference between the effective dose and a larger dose that can cause harm. A loading dose, to quickly raise the amount of the drug in the body, is recommended for injectable phenytoin and guidance on patient safety issues has previously been sissued.² Information on prescribing, preparation, administration and monitoring is available.^{3,4} and a decision should be taken locally on appropriate guidance for the use of phenytoin.

Injectable phenytoin is available in the strength of 50mg/mL and presented in a volume of 5mL. It may be administered undiluted or diluted only with sodium

Actions

Who: All organisations providing NHS-funded care where injectable phenytoin is prescribed, dispensed and/or administered.

When: To begin as soon as possible and to be completed by 21 December 2016.

Λ

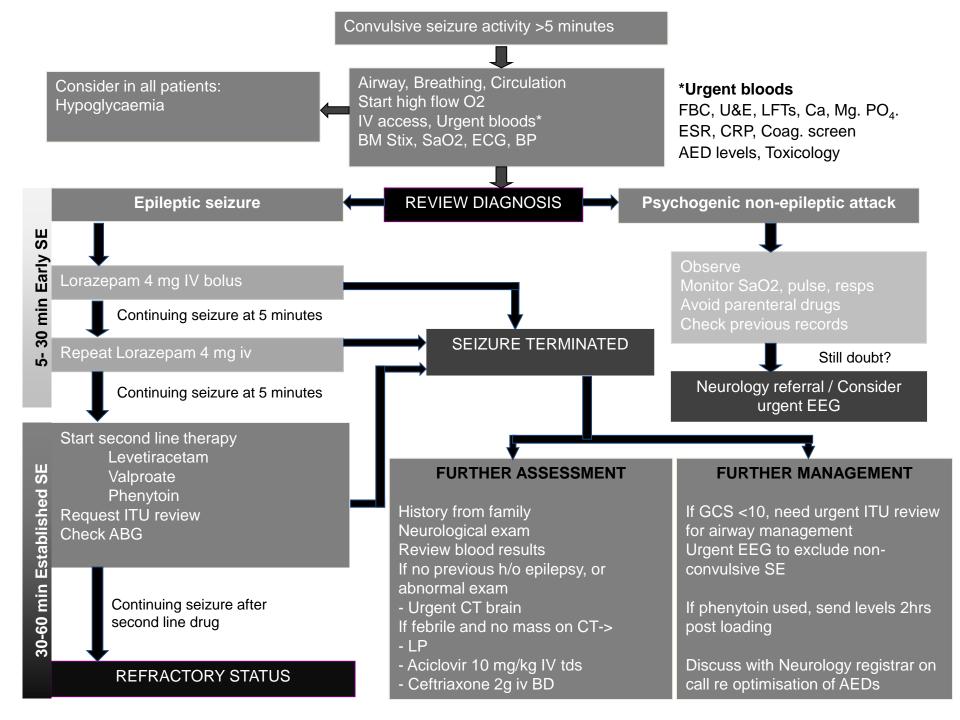
Other second line options

Phenobarbitone

- Usual IV loading dose 10 mg/kg @100 mg/min
 - Recent meta-analysis found 20mg/kg superior to VPA, LEV, PHT as second line
- Risk of sedation / respiratory depression when used after benzo
 - Meta-analysis showed no significant increase in AEs

Lacosamide

- Meta-analysis of second line treatments found 66% response rate
 - 400 mg IV loading, followed by 200 mg BD
 - Cardiac monitoring





Guideline for Management in Adults			
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ICU management of refractory status epilepticus

breakthrough seizures for 24 - 48 hours Maintain burst suppression with no

Convulsive seizure activity for 40 – 60 minutes, not terminated by IV lorazepam x 2 and second line agent (eg: IV valproate / levetiracetam)

> General anaesthesia with Propofol bolus, then continuous infusion Midazolam then continuous infusion

Intubate, ventilate, arterial line, central access Admit to ITU Observe for subtle convulsive activity Neurology review

Obtain urgent EEG to ensure electrographic seizures abolished and burst suppression achieved

If ongoing seizure activity - Thiopentone 3-5 mg/kg bolus, and continuous infusion (with monitoring)

Daily EEG recordings or continuous EEG monitoring Correct any metabolic derangement Ensure on adequate antiepileptic medication If on phenytoin, check level – consider further IV loading dose

Daily Bloods FBC, U&E, LFT, CRP, CK, Coagulation screen Phenytoin levels

Super refractory SE (SRSE)

- SE that recurs after 24 hours of general anaesthesia
- NORSE syndrome, FIRES, DESC
- High mortality (up to 50%)
 - 3rd line anaesthetic agents (ketamine, isoflurane)
 - Phenobarbitone, Magnesium, Topiramate
 - Immunotherapy (steroids, IVIg, PLEX, rituximab/tocilizumab)
 - Non pharmacological treatments (VNS, TMS, ketogenic diet)

Cases

Case 1

- 58 year old lady, cryptogenic left MCA stroke in 2018
- Witnessed by husband to suddenly become unresponsive, with a staring expression
- Brought in on the stroke pathway
- Seen in A&E 30min later ongoing twitching of hand and face, reduced responsiveness, intermittent vocalisation only

Q1. What is your diagnosis and management plan?

- 1. This is not status epilepticus; no intervention is required
- 2. This may be status epilepticus, EEG is needed for confirmation
- 3. This is status epilepticus, and should be treated as per status policy
- 4. This is status epilepticus, but **should not be** treated as per status policy

Table 2. Axis I: Classification of status epilepticus (SE)

(A) With prominent motor symptoms

A. I Convulsive SE (CSE, synonym: tonic-clonic SE)

A. I.a. Generalized convulsive

A. I.b. Focal onset evolving into bilateral convulsive SE

A. I.c. Unknown whether focal or generalized

A.2 Myoclonic SE (prominent epileptic myoclonic jerks)

A.2.a. With coma

A.2.b. Without coma

A.3 Focal motor

A.3.a. Repeated focal motor seizures (Jacksonian)

A.3.b. Epilepsia partialis continua (EPC)

A.3.c. Adversive status

A.3.d. Oculoclonic status

A.3.e. Ictal paresis (i.e., focal inhibitory SE)

A.4 Tonic status

A.5 Hyperkinetic SE

(B) Without prominent motor symptoms (i.e., nonconvulsive SE, NCSE)

B. I NCSE with coma (including so-called "subtle" SE)

B.2 NCSE without coma

B.2.a. Generalized

B.2.a.a Typical absence status

B.2.a.b Atypical absence status

B.2.a.c Myoclonic absence status

B.2.b. Focal

B.2.b.a Without impairment of consciousness (aura continua, with autonomic, sensory, visual, olfactory, gustatory, emotional/psychic/experiential, or auditory symptoms)

B.2.b.b Aphasic status

B.2.b.c With impaired consciousness

B.2.c Unknown whether focal or generalized

B.2.c.a Autonomic SE

Table 3. Currently indeterminate conditions (or "boundary syndromes")

Epileptic encephalopathies

Coma with non evolving epileptiform EEG pattern^a

Behavioral disturbance (e.g., psychosis) in patients with epilepsy

Acute confusional states, (e.g., delirium) with epileptiform EEG patterns

^aLateralized and generalized periodic discharges with monotonous appearance are not considered as evolving EEG patterns. ^{26,27}

Conceptual and pathophysiological definition of SE

Table 1. Operational dimensions with t_1 indicating the time that emergency treatment of SE should be started and t_2 indicating the time at which long-term consequences may be expected			
Type of SE	Operational dimension I Time (t ₁), when a seizure is likely to be prolonged leading to continuous seizure activity	Operational dimension 2 Time (t ₂), when a seizure may cause long term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits)	
Tonic-clonic SE	5 min	30 min	
Focal SE with impaired consciousness	10 min	>60 min	
Absence status epilepticus	I0–I5 min ^a	Unknown	
^a Evidence for the time frame is currently limited and future data may lead to modifications.			

Q2. How will you treat this patient?

- 1. IV lorazepam 4 mg
- 2. IV lorazepam 1 mg
- 3. Buccal midazolam 10 mg
- 4. Oral clobazam 10 mg
- 5. IV levetiracetam 4.5 gm

Classification by treatment approach

Supported by class 1 evidence (Status policy)

- A. I Convulsive SE (CSE, synonym: tonic-clonic SE)
 - A. I.a. Generalized convulsive
 - A. I.b. Focal onset evolving into bilateral convulsive SE
 - A.I.c. Unknown whether focal or generalized
- A.2 Myoclonic SE (prominent epileptic myoclonic jerks)
 - A.2.a. With coma
 - A 2 h Without coma

Started as GCSE

Treat as per SE policy

A 3 h Enilancia partialis continua (EPC)

No history of GCSE

Probably treat as per SE policy

A.3.e. Ictal paresis (i.e., focal inhibitory SE)

- A.4 Tonic status
- A.5 Hyperkinetic SE

No class I evidence to guide treatment

- B. I NCSE with coma (including so-called "subtle" SE)
- B.2 NCSE without coma
 - B.2.a. Generalized
 - B.2.a.a Typical absence status
 - B.2.a.b Atypical absence status
 - B.2.a.c Myoclonic absence status
 - B.2.b. Focal

В.

Lower risk of neuronal damage from prolonged episodes than GCSE

D.Z.D.D Apnasic status

Risks of aggressive treatment may not be justifiable

Table 3. Currently indeterminate conditions (or "boundary syndromes")

Epileptic encephalopathies

Coma with non evolving epileptiform EEG pattern^a

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'Non-convulsive status epilepticus'

- Describes a wide variety of clinical states
 - 'True' non convulsive status (absence, focal aware / unaware)
 - Advanced convulsive status
 - Boundary syndromes
- True NCSE (absence SE, focal SE)
 - No class 1 evidence to guide treatment
 - No evidence that absence SE leads to neuronal damage
 - Focal (aware/ unaware) SE in patients with epilepsy probably associated with low risk of neurological decline
 - Aggressive treatment, particularly in the elderly, may be associated with worse outcomes
 - Focal SE in patients with acute brain insults associated with worse outcomes
 - Unclear if aggressive treatment of seizures improves outcomes

General anaesthesia and outcomes of SE

Anesthetic Drugs in Status Epilepticus: Risk or Rescue? A 6-Year Cohort Study.

Sutter R, Marsch S, Fuhr P, Kaplan PW, Rüegg S. Neurology 2014 Feb 25;82:656-664.

results regarding the risk

ings heighten awareness

the association of IVADs

evidence that patients w

compared to patients no

OBJECTIVE: To evaluate the risks of continuously administered IV anesthetic drugs (IVADs) on the outcome of adult patients with status epilepticus (SE). METHODS: All intensive care unit patients with SE from 2005 to 2011 at a tertiary academic medical care center were included. Relative risks were calculated for the primary outcome measures of seizure control, Glasgow Outcome Scale score at discharge, and death. Poisson regression models were used to control for possible confounders and to assess effect modification. RESULTS: Of 171 patients, 37% were treated with IVADs. Mortality was 18%. Patients with anesthetic drugs had more infections during SE (43% vs 11%; p < 0.0001) and a 2.9-fold relative risk for death (2.88; 95% confidence interval 1.45–5.73), independent of possible confounders (i.e., duration and severity of SE, nonar activate third line antiquipatic damage and critical modical conditions) and without cignificant

effect modification by di Status Epilepticus: Impact of Therapeutic Coma on Outcome.

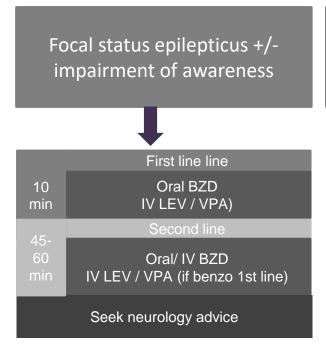
drugs failed, there was a Marchi NA, Novy J, Faouzi M, Stähli C, Burnand B, Rossetti AO. Crit Care Med 2015;43:1003–1009.

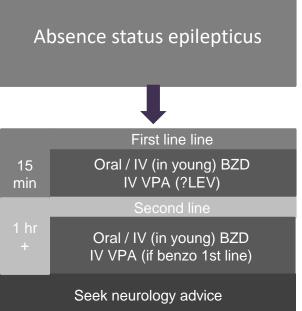
OBJECTIVES: Therapeutic coma is advocated in guidelines for management of refractory status epilepticus; this is, however, based on weak evidence. We here address the specific impact of therapeutic coma on status epilepticus outcome. DESIGN: Retrospective assessment of a prospectively collected cohort. SETTING: Academic hospital. PATIENTS: Consecutive adults with incident status epilepticus lasting greater than or equal to 30 minutes, admitted between 2006 and 2013. MEASUREMENTS AND MAIN RESULTS: We recorded prospectively demographics, clinical status epilepticus features, treatment, and outcome at discharge and retrospectively medical comorbidities, hospital stay, and infectious complications. Associations between potential predictors and clinical outcome were analyzed using multinomial logistic regressions. Of 467 patients with incident status epilepticus, 238 returned to baseline (51.1%), 162 had new disability (34.6%), and 67 died (14.3%); 50 subjects (10.7%) were managed with therapeutic coma. Therapeutic coma was associated with poorer outcome in the whole cohort (relative risk ratio for new disability, 6.86; 95% Cl, 2.84-16.56; for mortality, 9.10; 95% CI, 3.17–26.16); the effect was more important in patients with complex partial compared with generalized convulsive or nonconvulsive status epilepticus in coma. Prevalence of infections was higher (odds ratio, 3.81; 95% Cl, 1.66–8.75), and median hospital stay in patients discharged alive was longer (16 d [range, 2–240 d] vs 9 d [range, 1–57 d]; p < 0.001) in subjects managed with therapeutic coma. CONCLUSIONS: This study provides class III evidence that therapeutic coma is associated with poorer outcome after status epilepticus; furthermore, it portends higher infection rates and longer hospitalizations. These data suggest caution in the straightforward use of this approach, especially in patients with complex partial status epilepticus.

Treatment of non-convulsive status epilepticus

A proposed protocol

EEG confirmation mandatory in all situations apart from focal motor status (EPC)





Coma Evolved from GCSE (subtle CSE)

Coma with no previous CSE

Should be managed as per status epilepticus policy with GA to achieve burst suppression

Where possible, avoid IV BDZ in older adults. In general, risks of general anaesthesia outweigh risks of potential neuronal damage in focal and absence SE

Case 2

- A 90 year old lady, nursing home resident, was admitted with suspected respiratory infection
- At admission she was febrile, confused and had a CRP of 25
- She was started on antibiotics, but the following day was still febrile and more drowsy. CT brain and LP were unremarkable
- Your colleague requests an EEG

"Interpretation of this EEG is dependent on the clinical picture.

C4

P4 -FP1 A-F7 -T3 -

T5 -FP1

F3

C3

There is evidence of global cortical dysfunction. The sharp and slow complexes that are asymmetrical, maximal over the right temporal or temporo-parietal region, which would indicate a liability to seizures, and seizures may be contributing to the patients clinical features.

This EEG could even reflect non-convulsive status epilepticus.

There is a periodic nature to the discharges, and depending on the clinical picture, the electrographic abnormalities could also raise the possibility of a prion disorder"

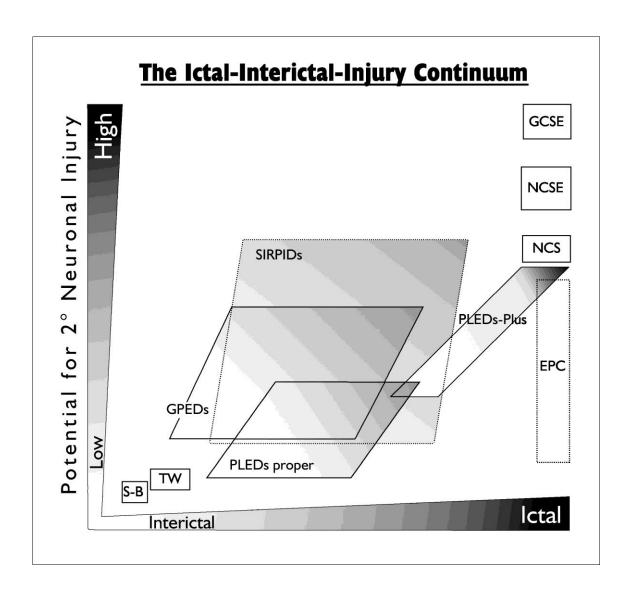
Q3. What management will you advise?

- "Load with IV Valproate"
- 2. "Try and give some oral Clobazam"
- 3. "Get an MRI to look for DWI changes of CJD"
- 4. "Ignore the EEG?"

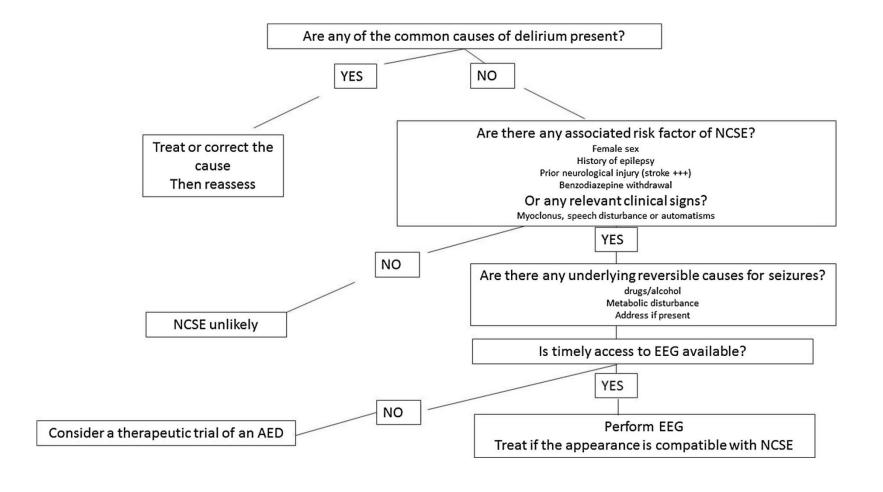
CRP 326

Diagnosis: Sepsis Associated Encephalopathy

What is a seizure?



Elderly with encephalopathy Approach to ?NCSE



Conclusions

- There is an evidence based policy for management of convulsive SE
- 'Non convulsive SE' is a non specific term that needs to be interpreted in the correct context
 - It is over-diagnosed, mainly due to misinterpretation of EEG reports
 - Neurologists have a key role in interpreting EEG findings in clinical context
 - Aggressive treatment of focal / absence SE may be associated with worse outcomes