NEANU
North of England
Acute Neurology
Update

Confusion... 5 things...

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Disclosures

- Honoraria received for educational talks from Eisai, Biogen
- BMJ Best Practice expert advisor

5 Things...

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- Confusion is difficult
- Time course is critical
- Recognition and localization
- What about investigations?
- When do I worry about encephalitis?

Number 1

- Confusion is difficult…

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- alteration in mental status affecting the patient's cognition or level of arousal

- mental status changes due to focal or global brain insults

- **Vascular/Ischemic**
  - Multi-infarct
  - Thalamic or callosum infarcts
  - Cerebral amyloid angiopathy
  - Dural arteriovenous fistulas
  - Central nervous system (CNS) vasculitis
  - Venous thrombosis
  - Cerebroretinal microangiopathy with calcifications and cysts
  - Posterior reversible encephalopathy syndrome (PRES)
  - Subacute diencephalic angioencephalopathy
- **Infectious**
  - Viral encephalitis, including herpes simplex virus
  - Human immunodeficiency virus dementia
  - Progressive multifocal leukoencephalopathy
  - Fungal infections (eg, CNS aspergillosis, coccidioidomycosis)
  - Amoebic infection (eg, *Balamuthia mandrillaris*)
  - Spirochete infection
  - Lyme disease (rarely encephalopathy)
  - Whipple disease (rarely rapid)
  - Subacute sclerosing panencephalitis (young adults)
  - Urinary tract infection, pneumonia in elderly patient or patient with mild dementia
- **Toxic-Metabolic**
  - Electrolyte disturbances (sodium, calcium, magnesium, phosphorus)
  - Endocrine abnormalities (thyroid, parathyroid, adrenal)
  - Extrapontine myelinolysis
  - Vitamin B_{12} (cyanocobalamin) deficiency
  - Vitamin B_1 (thiamine) deficiency (Wernicke encephalopathy)
  - Niacin deficiency (not usually rapid)
  - Folate deficiency (dementia rare)
  - Uremic encephalopathy
  - Portosystemic shunt encephalopathy
  - Poikilothermia

Continued on

  - Hepatic encephalopathy
  - Acquired hepatocerebral degeneration
  - Hypoxia/hypercarbia
  - Hyperglycemia/hypoglycemia
  - Porphyria
  - Metal toxicity (bismuth, lithium, mercury, magnesium [Parkinsonisr
  - Mitochondrial disease (eg, mitochondrial myopathy, encephalopathy acidosis, and strokelike episodes syndrome [MELAS])
- **Autoimmune**
  - Antibody-mediated dementia/encephalopathy
  - CNS lupus
  - Acute disseminated encephalomyelitis (ADEM)
  - Hashimoto encephalopathy (steroid-responsive encephalopathy associated with autoimmune thyroiditis [SREAT])
  - Other CNS vasculitides
- **Metastases/Neoplasm Related**
  - Paraneoplastic diseases—limbic encephalopathy
  - Metastases to CNS
  - Primary CNS lymphoma
  - Intravascular lymphoma
  - Lymphomatoid granulomatosis
  - Lymphomatosis cerebri
  - Gliomatosis cerebri
  - Metastatic encephalopathy
  - Carcinomatous meningitis
- **Iatrogenic**
  - Medication toxicity (eg, lithium, methotrexate, chemotherapy)
  - Illicit drug use
- **Neurodegenerative**
  - Prion disease
  - Alzheimer disease
  - Dementia with Lewy Bodies
  - Frontotemporal dementia
  - Corticobasal degeneration

Continued on page 521

  - Progressive supranuclear palsy
  - Neurofilament inclusion body disease
  - Progressive subcortical gliosis
- **Systemic/Seizures/Structural**
  - Sarcoidosis
  - Epilepsy
  - Nonconvulsive status epilepticus
  - Subdural hematoma
  - Mitochondrial disease (eg, MELAS)

Back to Basics

History

Examination

Standardised approach

+

Specific clues

Investigations

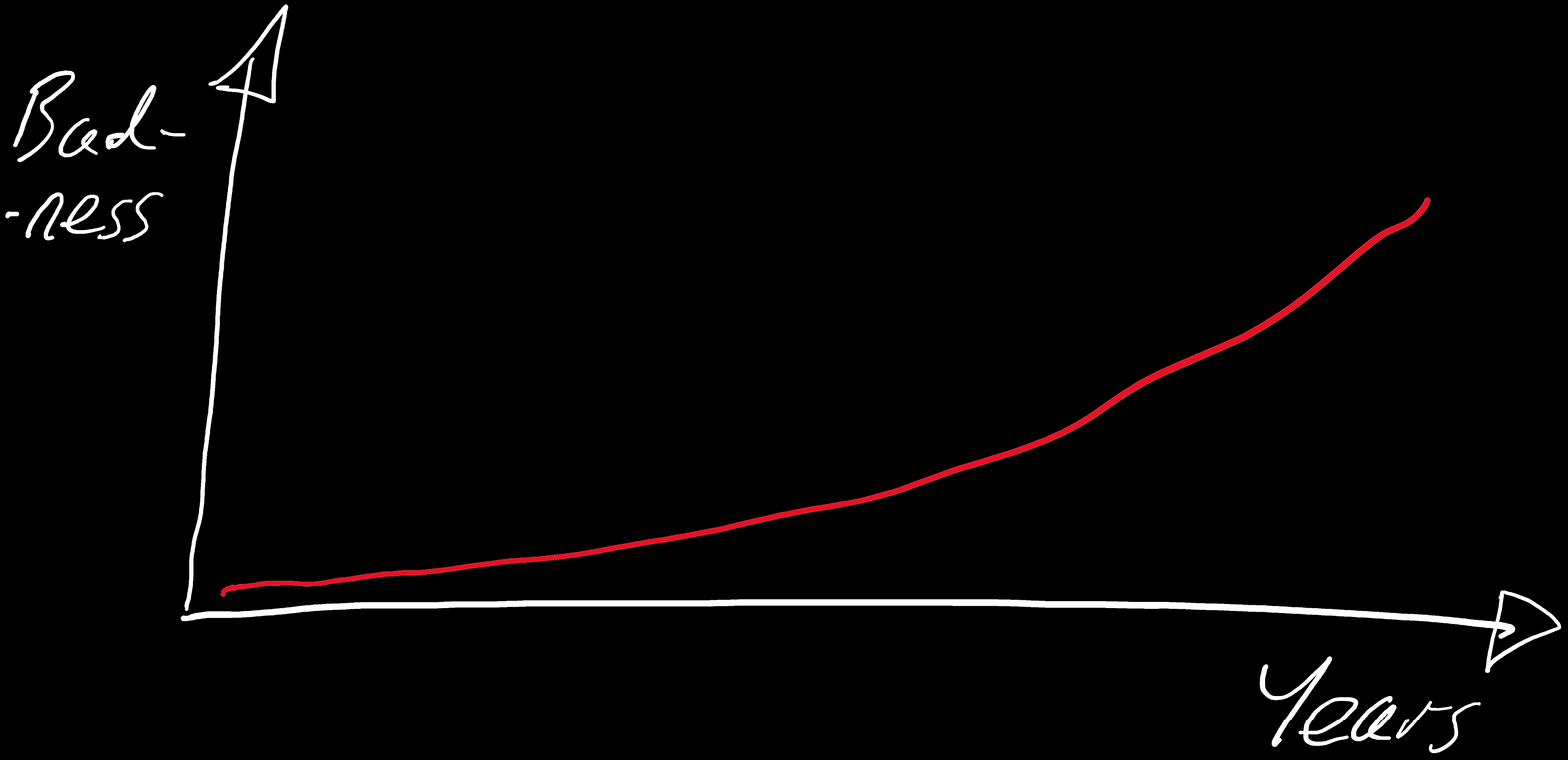
Systemic	Brain
Basic bloods	MRI
+	CSF
imaging	EEG

	Hyperacute	Acute	Subacute	Chronic
Focal (1ry brain)				
Global (systemic)				

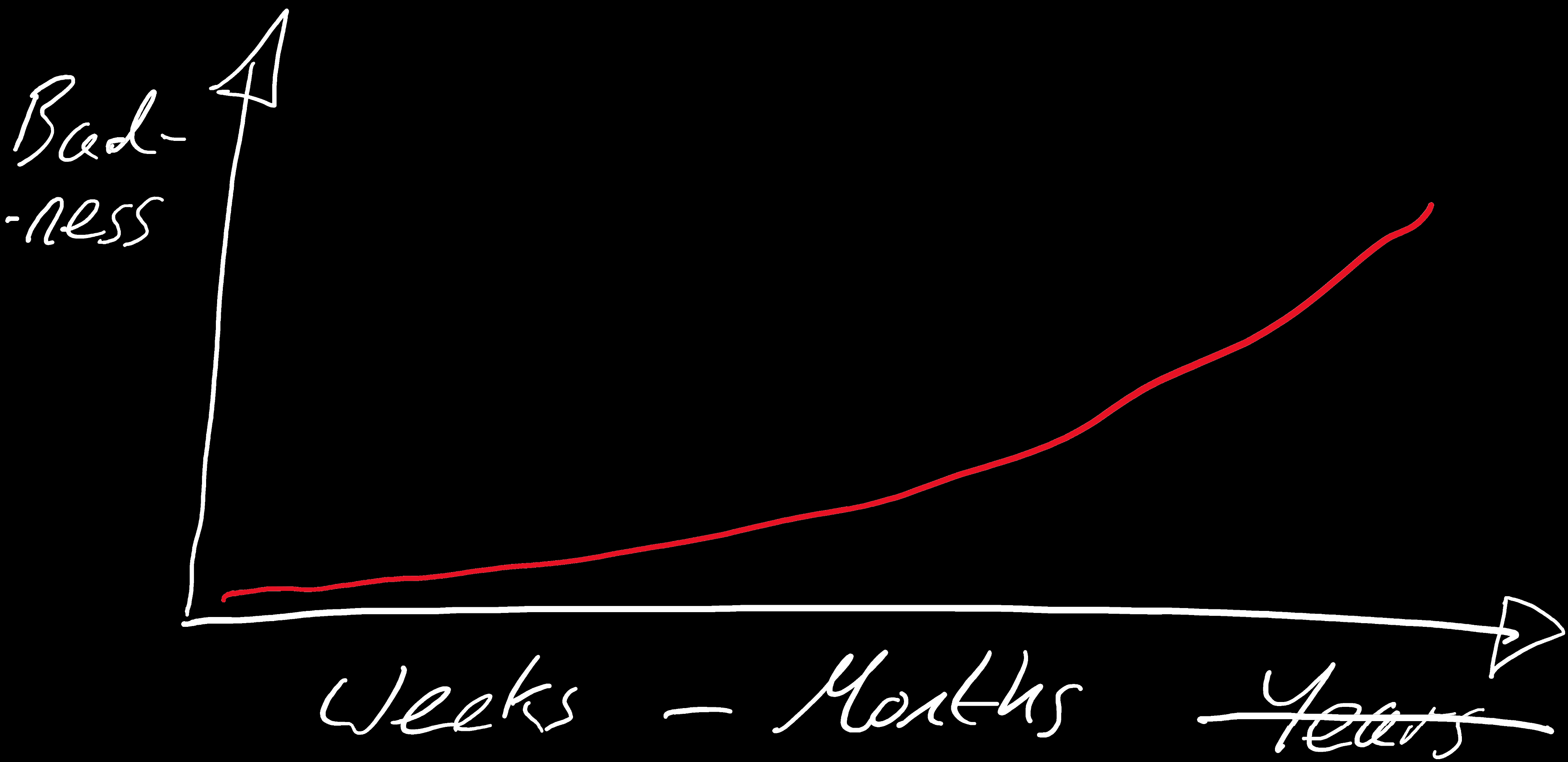
Number 2

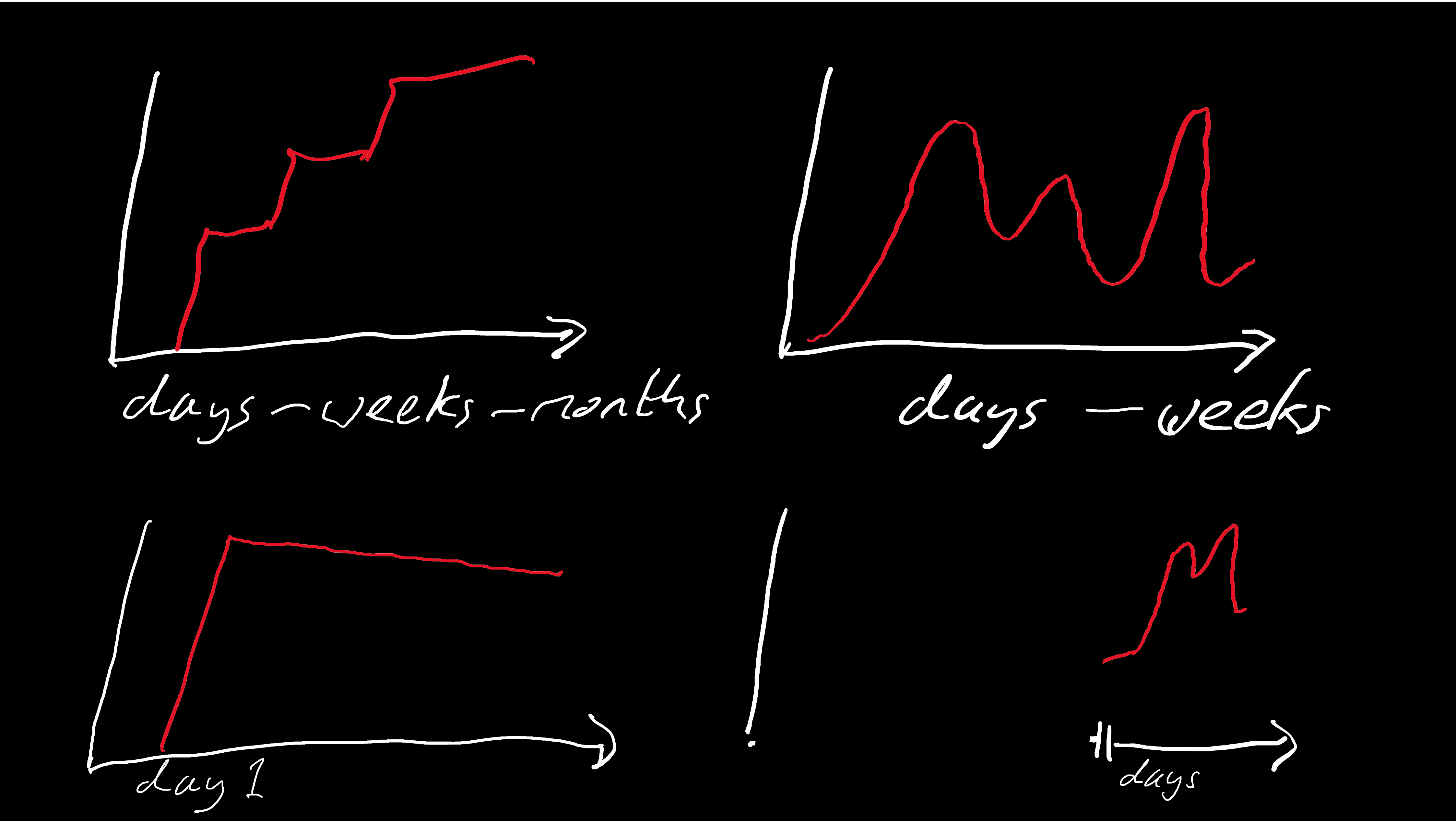
- Time course is critical…

Back to Basics



Back to Basics



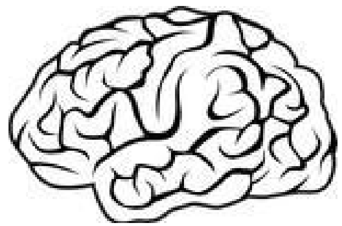

days – weeks – months
days – weeks
day 1
days

Number 3

- Recognition and localization...
- Primary brain vs systemic
- Focal vs global

Recognising the syndrome

- Hypoactive / hyperactive / disinhibited
- Purposeless / disorganised



- Disorientated in time
- Incoherent / unable to follow commands / poor writing
- Disorientated spatially / visual illusions / hallucinations

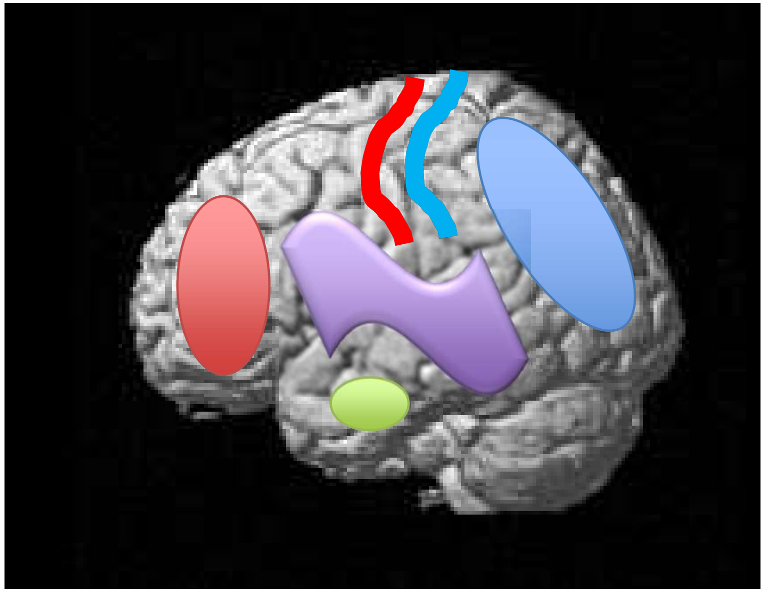
Recognising the syndrome

- Behaviour
  - Hypoactive / hyperactive / disinhibited
- Executive
  - Purposeless / disorganised
- Memory
  - Disorientated in time
- Language
  - Incoherent / unable to follow commands / poor writing
- Visuo-spatial
  - Disorientated spatially / visual illusions / hallucinations

Language

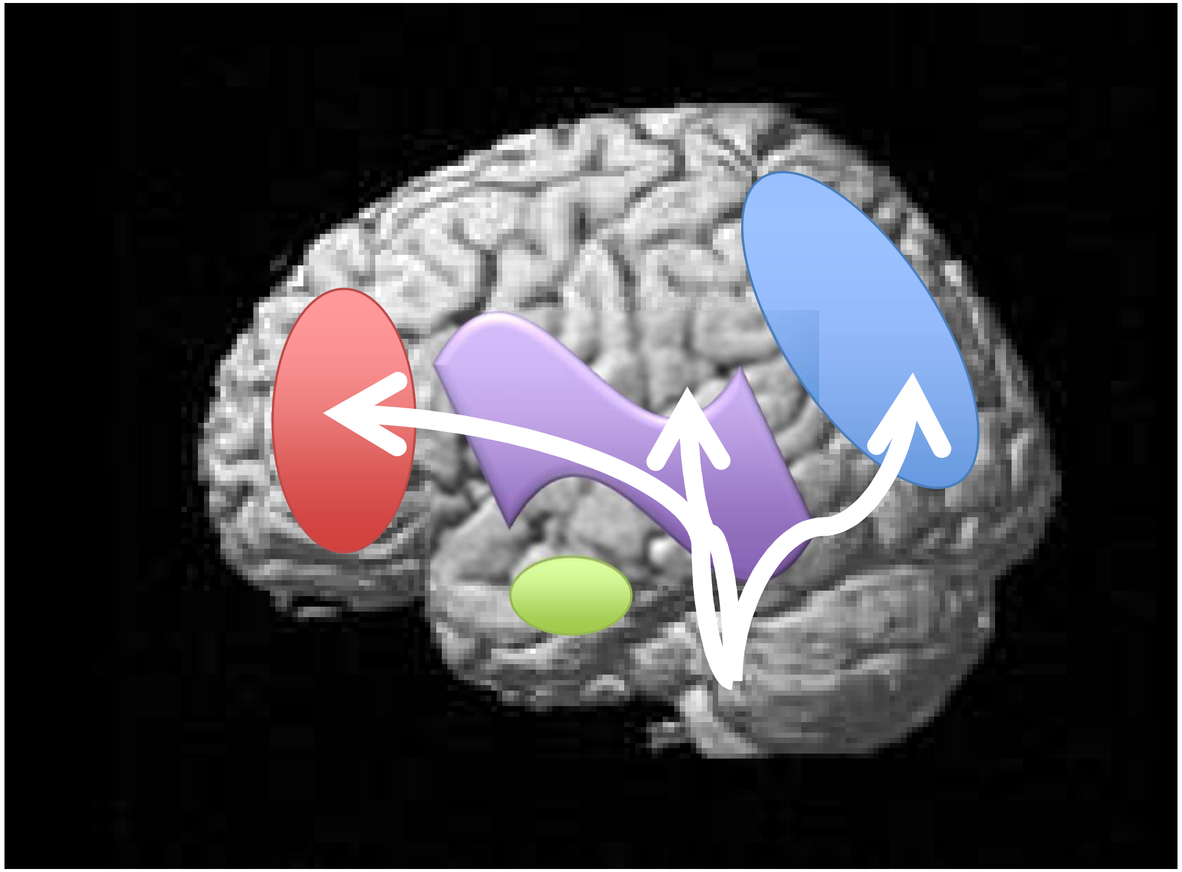
Production Understanding

Behaviour
Executive



Visuo-spatial
function

Memory



Focal/brain

- Hemiparesis
- Aphasia
- Amnesia
- Seizures/mvmt disorder
- Headache

- No systemic clues

Global/Systemic

- Altered arousal
- Fluctuation
- Altered perception
- Lack of focal signs
- Risk groups

- Systemic clues

Examples

Focal

- Infection
  - HSV
  - HIV (or opportunistic)
  - Syphilis
- Inflammation
  - Vasculitis / demyelination
  - Limbic encephalitis
- Neoplasia
  - Metastasis
  - Brain 1ry
- Degeneration
  - Lewy Body Disease
  - Prion Disease
- Bleeding
  - ICH
  - Subdural haematoma

Global

- Sepsis
- Hepatic
- Renal
- Endocrine/biochem
  - Na, Ca, glucose, T4
- Cardio-respiratory
  - Hypoxia
  - Hypercapnia
- Toxic
  - Alcohol, drugs
- Nutritional
  - B1, B12

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	Hyperacute	Acute	Subacute	Chronic
Focal (1ry brain)	ICH Isch stroke	Inf enceph Vasculitis SDH	AI enceph Neoplasia SDH	DLB
Global (systemic)	Cardioresp	Cardioresp Sepsis Endo/bioch	Nutritional Toxic Endo/bioch	Toxic

Number 4

- How does all this affect investigations..?

Focal/brain

- Likely to need
  - Acute / detailed neuroimaging
  - +/- CSF analysis
  - +/- EEG
  - +/- Fancy blood tests
- 'Routine' blood work likely to be **normal**

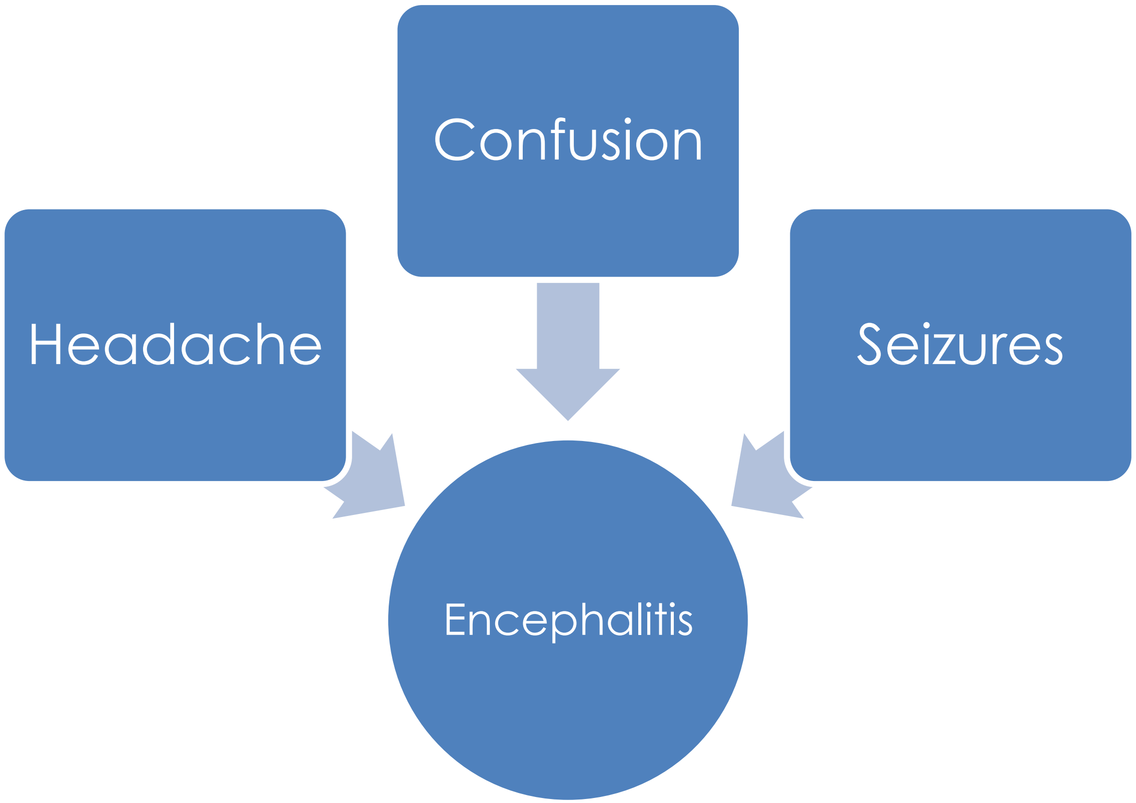
Global/Systemic

- Unlikely to require:
  - Detailed neuroimaging
  - CSF analysis
  - EEG
  - Fancy blood tests
- 'Routine' blood work more likely **abnormal**

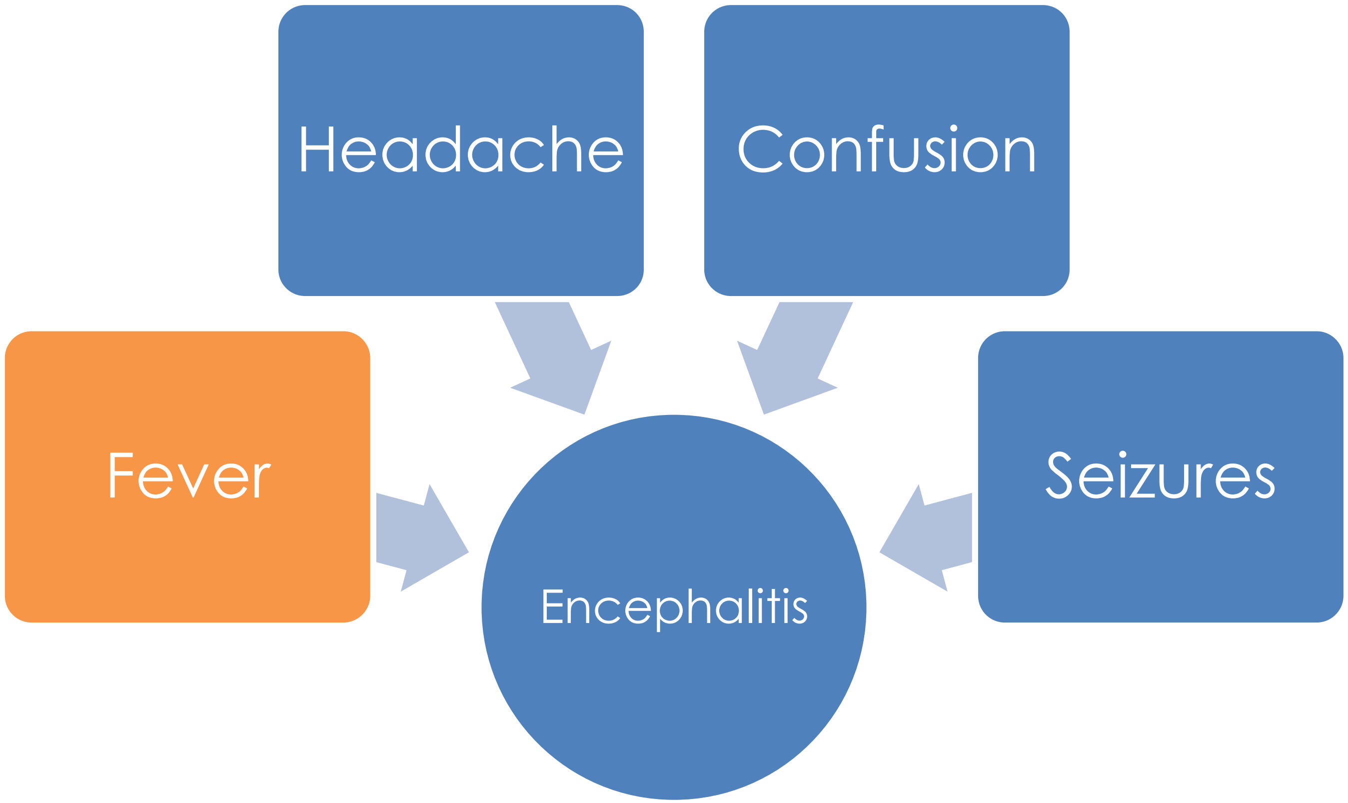
Number 5

- When do I worry about encephalitis?

Encephalitis



Infective



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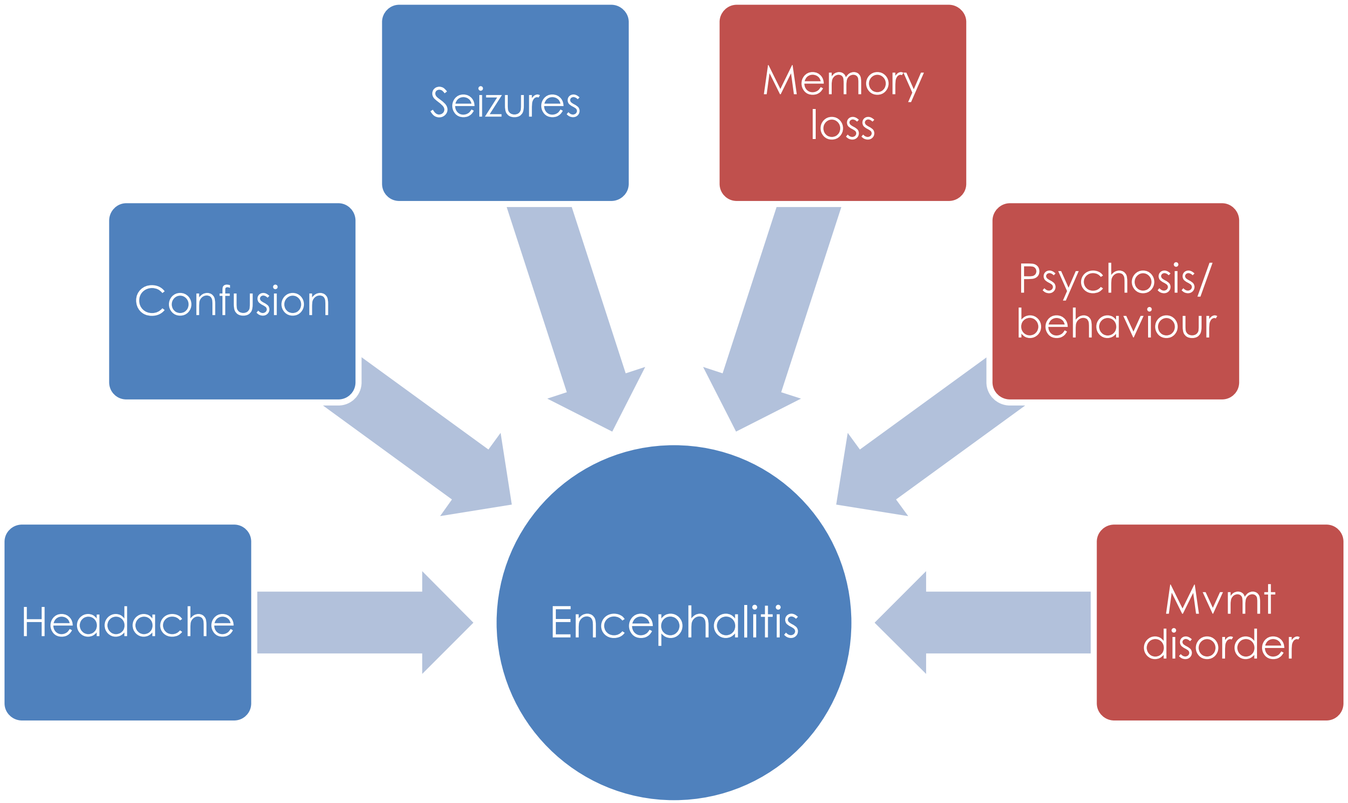
ROUGH
GUIDES

Antibody mediated



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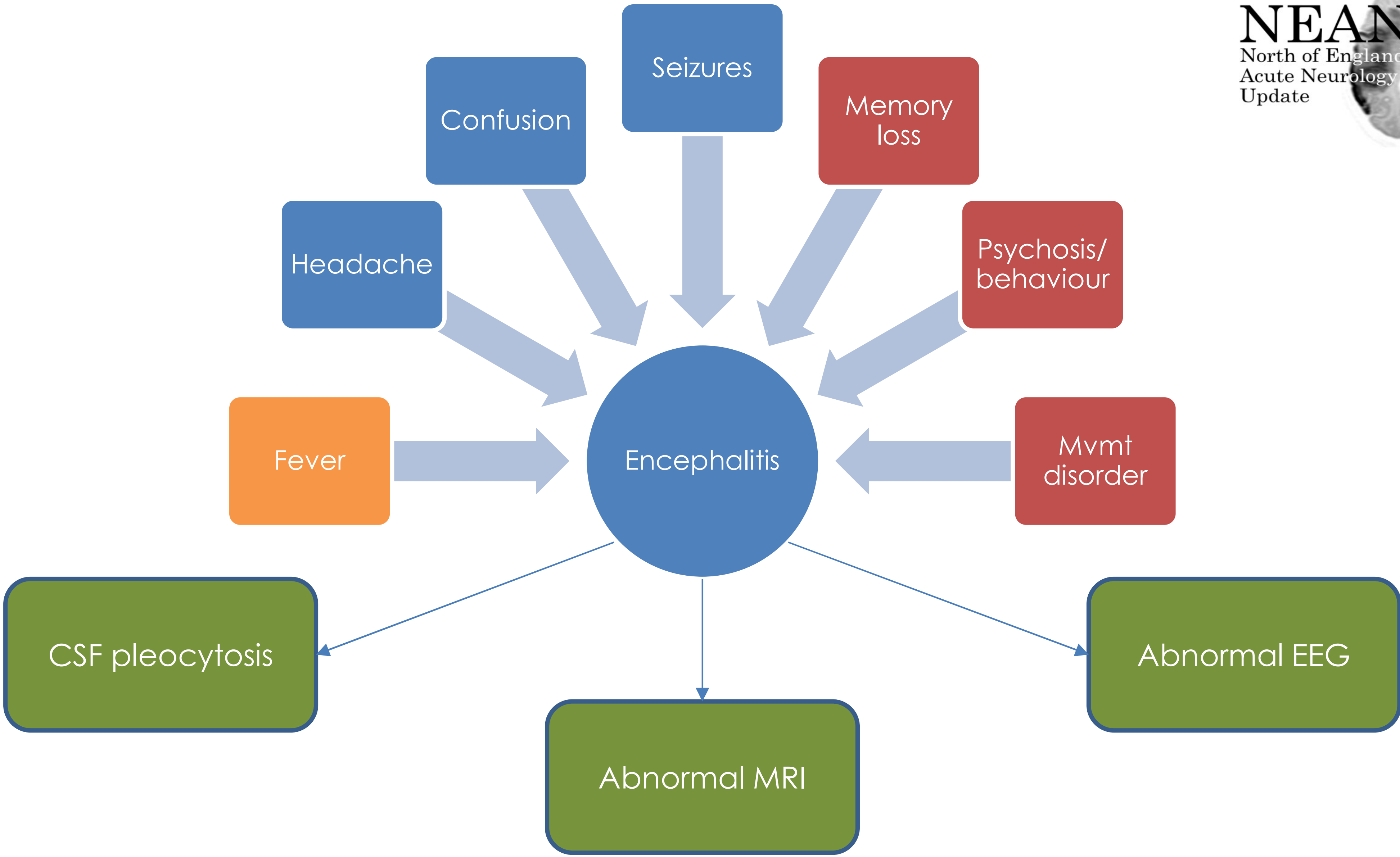

Encephalitis… a less rough guide…

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Major Criterion (required):
Patients presenting to medical attention with altered mental status (defined as decreased or altered level of consciousness, lethargy or personality change) lasting ≥24 h with no alternative cause identified.
Minor Criteria (2 required for possible encephalitis; ≥3 required for probable or confirmed[a] encephalitis):
Documented fever ≥38° C (100.4°F) within the 72 h before or after presentation[b]
Generalized or partial seizures not fully attributable to a preexisting seizure disorder[c]
New onset of focal neurologic findings
CSF WBC count ≥5/cubic mm[d]
Abnormality of brain parenchyma on neuroimaging suggestive of encephalitis that is either new from prior studies or appears acute in onset[e]
Abnormality on electroencephalography that is consistent with encephalitis and not attributable to another cause.[f]

Consensus Document on Encephalitis • **CID 2013:57 (15 October)**

The commonest causes

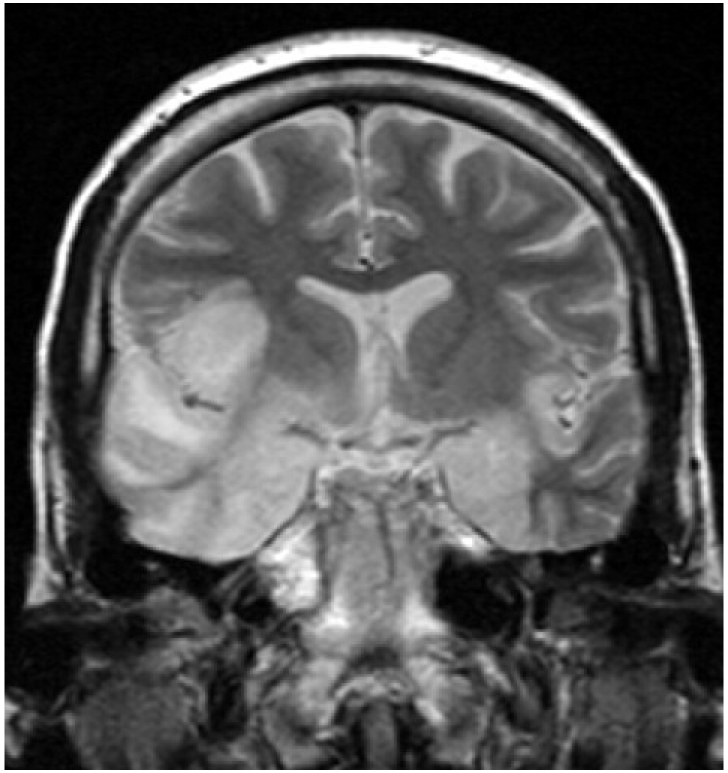
Viral

Immunocompetent

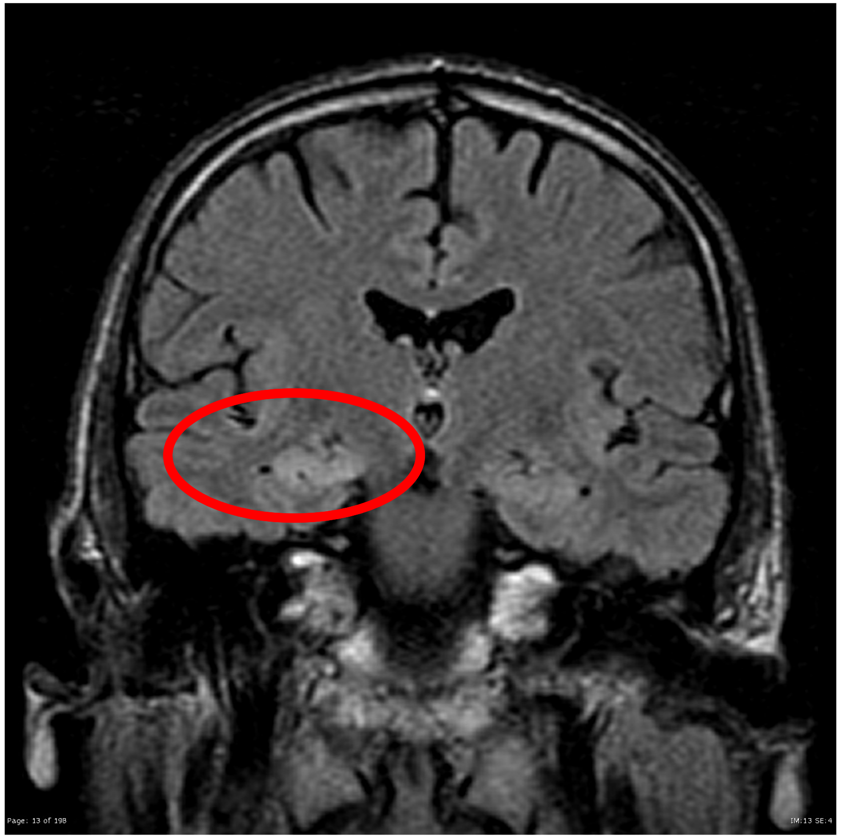
- Herpes simplex type I
- VZV

Immunocompromised

- HIV
- CMV, JC, HHV6, toxo,



The commonest causes



Antibodies

Neuronal surface antigen
- LGI1, CASPR2, NMDAr
- GABA, AMPA

Intracellular antigen
- Hu, CV2, Ma1/2,
- GAD

JAMA Neurology | Original Investigation

Autoimmune Encephalitis Misdiagnosis in Adults

Eoin P. Flanagan, MD; Michael D. Geschwind, MD, PhD; A. Sebastian Lopez-Chiriboga, MD; Kyle M. Blackburn, MD; Sanchit Turaga, MD; Sophie Binks, MD; Jennifer Zitser, MD; Jeffrey M. Gelfand, MD; Gregory S. Day, MD; S. Richard Dunham, MD; Stefanie J. Rodenbeck, MD; Stacey L. Clardy, MD, PhD; Andrew J. Solomon, MD; Sean J. Pittock, MD; Andrew McKeon, MD; Divyanshu Dubey, MD; Anastasia Zekeridou, MD, PhD; Michel Toledano, MD; Lindsey E. Turner; Steven Vernino, MD, PhD; Sarosh R. Irani, MD, DPhil

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Table 1. Alternative Final Diagnoses in Those Initially Misdiagnosed as Autoimmune Encephalitis

Alternative diagnosis	No. (%) Individuals with initial diagnosis (n = 107)	No. (%) Individuals who fulfilled possible autoimmune encephalitis criteria (n = 30)
Functional neurologic disorder	27 (25)	6 (22)
Neurodegenerative dementia	22 (20.5)	5 (23)
Alzheimer disease[a]	6	0
Dementia with Lewy bodies[b]	4	1
Behavioral variant frontotemporal dementia	4	2
Creutzfeldt-Jakob disease	2	1
Vascular cognitive impairment	1	0
Other[c]	5	1[c]
Psychiatric disease	19 (18)	2 (11)
Depression[d]	7	2
Anxiety	3	0
Schizophrenia	2	0
Bipolar	2	0
Other[e]	5	0
Nonspecific cognitive syndrome in the setting of ≥1 of fibromyalgia, chronic fatigue, sleep disorder, medication adverse reaction, or other comorbidity[f]	11 (10)	1 (9)[f]
Neoplasm	10 (9.5)	7 (70)
Glioma (glioblastoma, astrocytoma, or not otherwise specified)[g]	7	5
Primary central nervous system lymphoma	2	2
Cerebellar medulloblastoma with cerebellar cognitive syndrome	1	0
Seizure disorder, nonimmune-mediated[h]	5 (4.5)	3 (60)
Infectious	3 (2.5)	1 (33)

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Possible Autoimmune Encephalitis

Questions