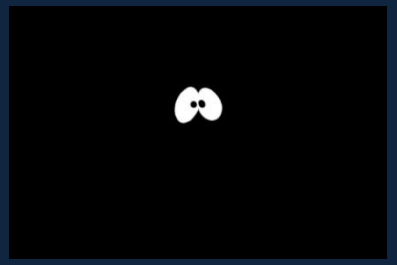
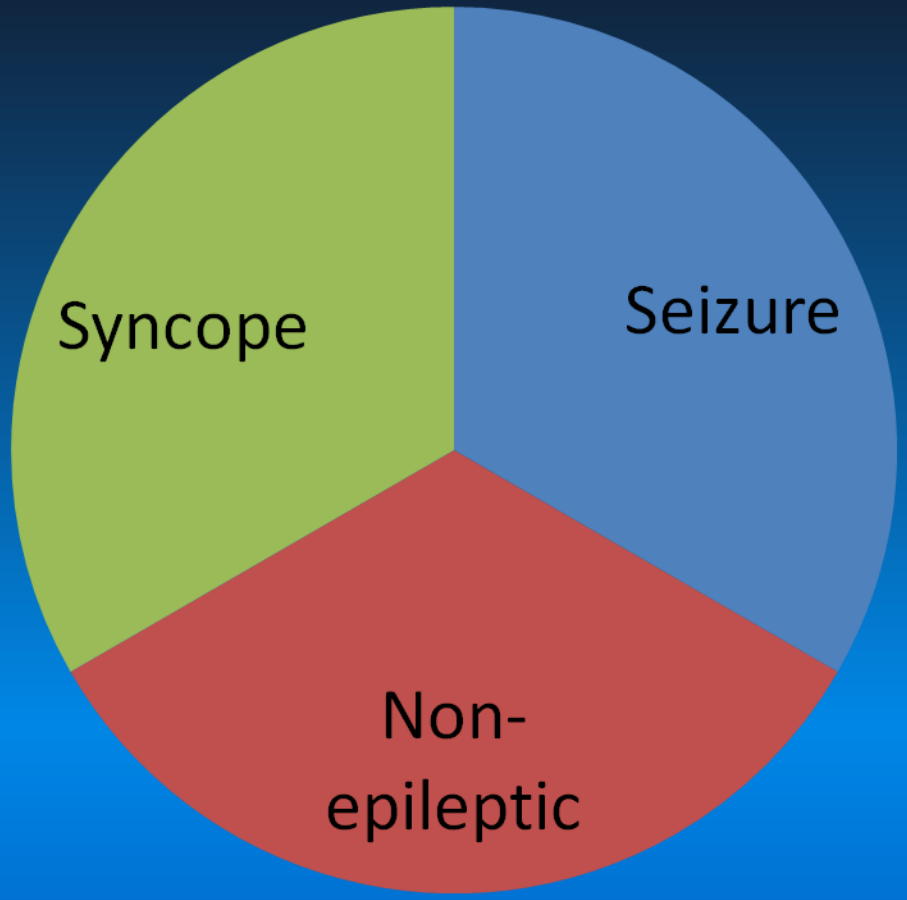
BLACKOUTS AND EPILEPSY

DR STEPHAN HINZE

GREAT WESTERN HOSPITAL, SWINDON

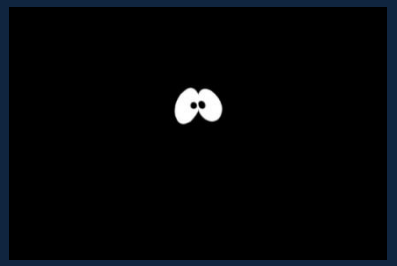


Blackouts



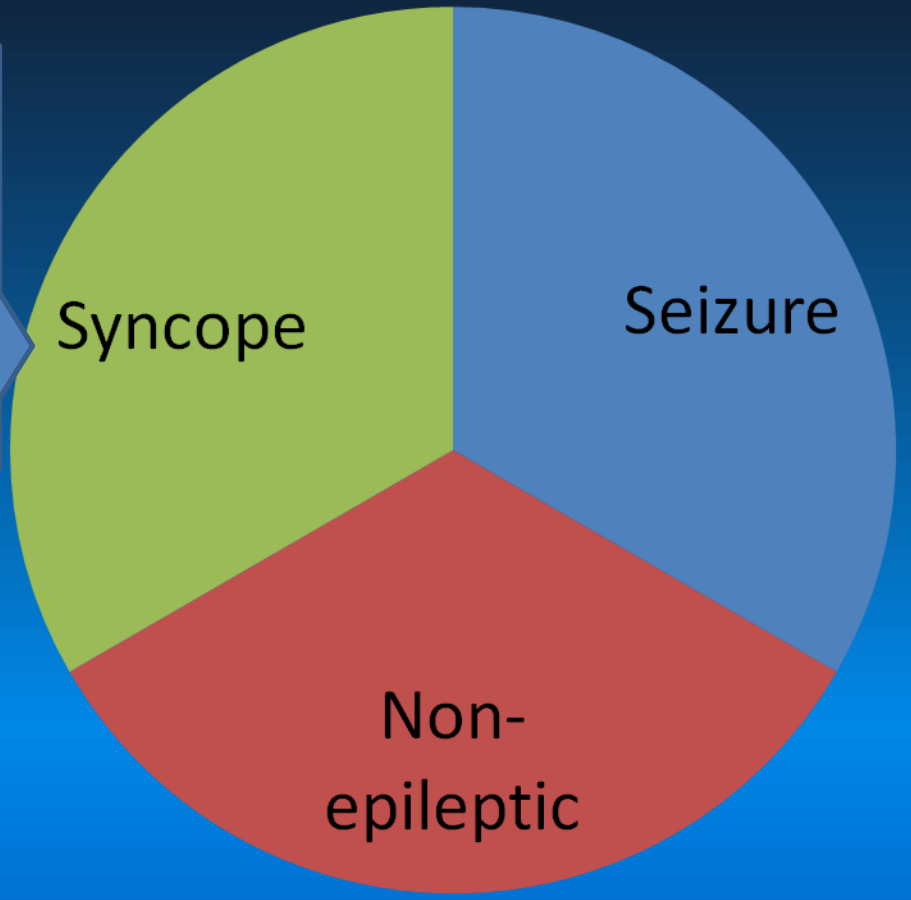
LOC/LOA and the DVLA

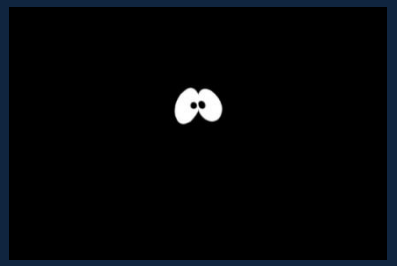
	Group 1 (car)	Group 2 (bus/lorry)
1st unprovoked Seizure	6 months	5 years
Typical vasovagal (*standing*) (3 Ps: provocation, prodrome, postural)	-	DVLA
Syncope with avoidable trigger (*sitting*)	1 month	3 months
Likely cardiovascular	6 months (4 weeks if treated)	12 months (3 months if treated)
Unexplained syncope	6 months	12 months
>2x unexplained syncope	12 months	10 years
Epilepsy	12 months	10 years (w/o AEDs)
Epilepsy – AED withdrawal	Until 6 months post cessation	



Blackouts

Prolonged upright position
Pre-syncopal symptoms
Pallor





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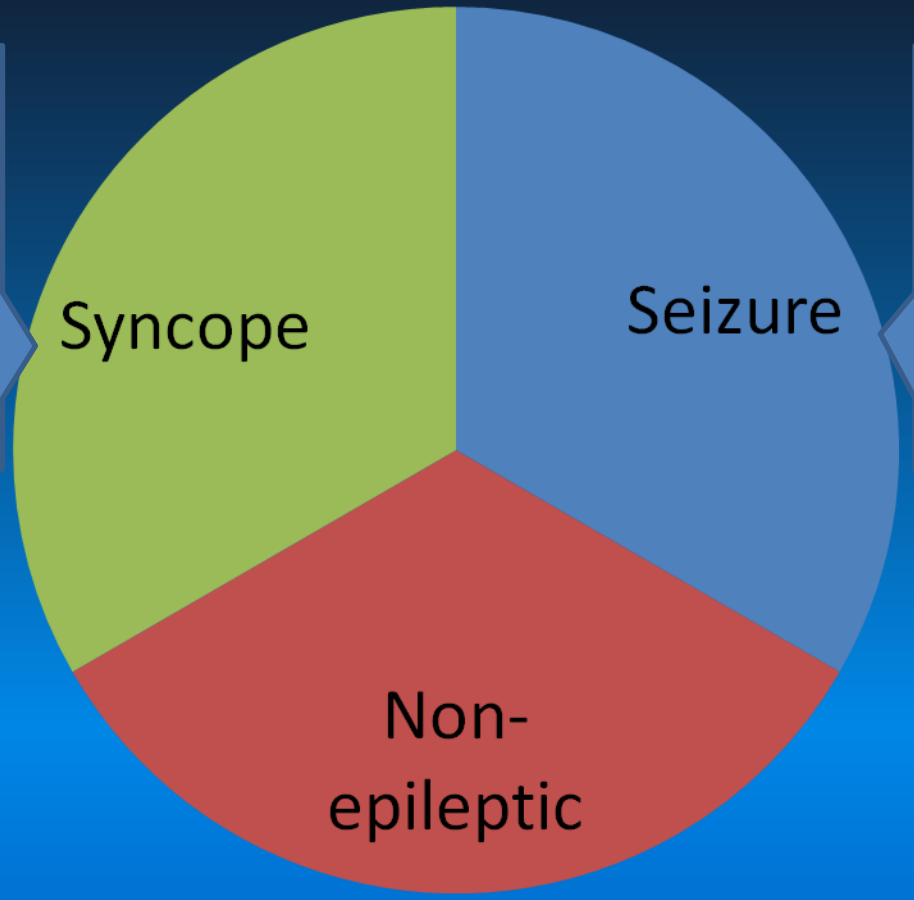
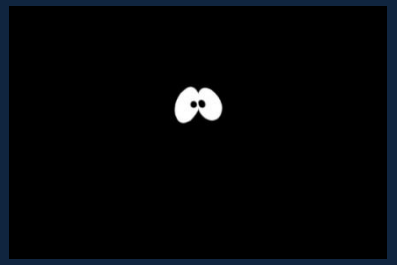


Cyanosis
LOC for minutes
Post-ictal confusion
Lateral tongue bite



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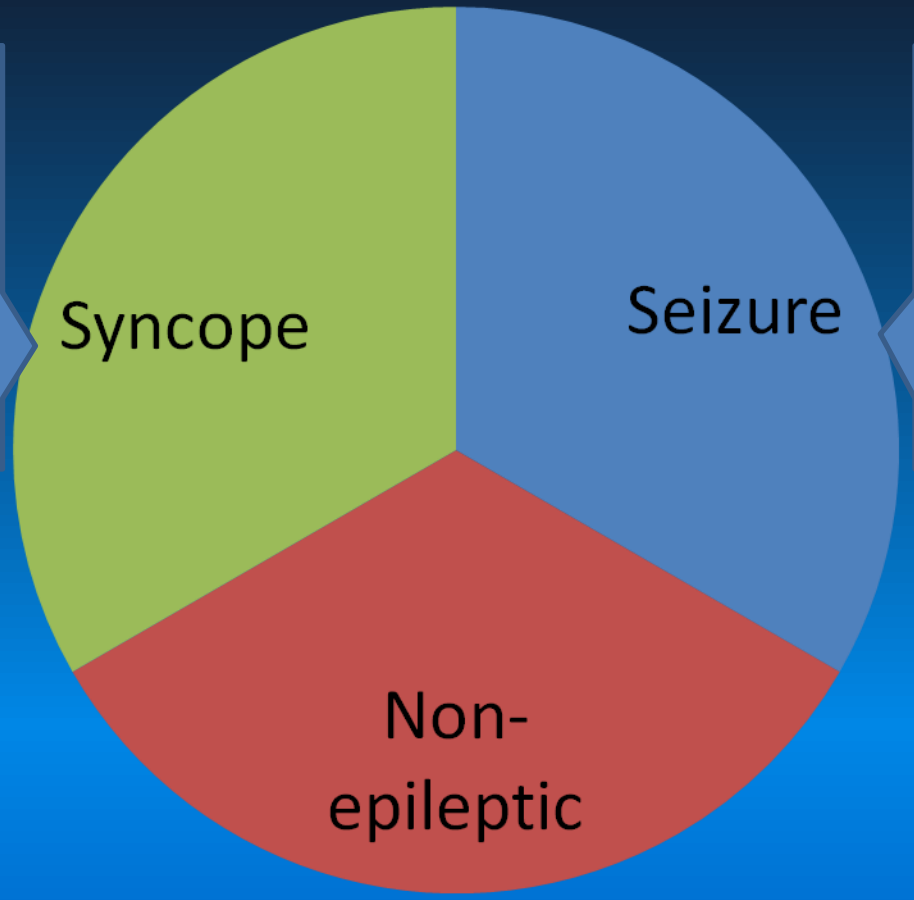


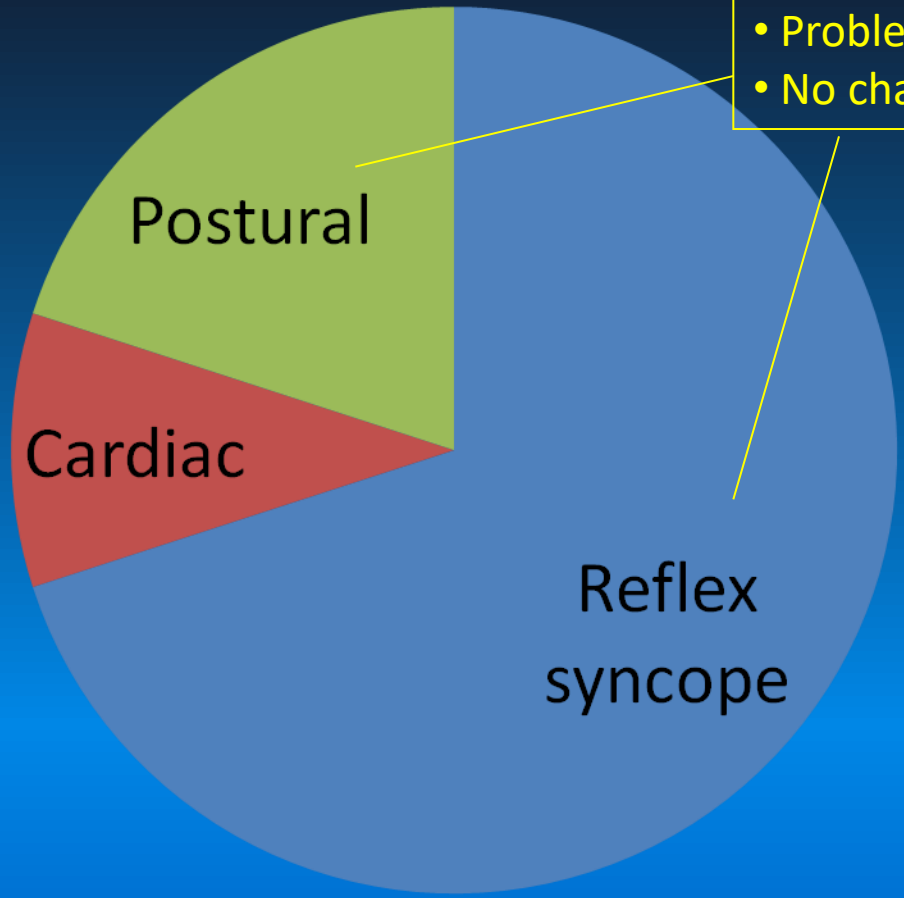
Cyanosis
LOC for minutes
Post-ictal confusion
Lateral tongue bite

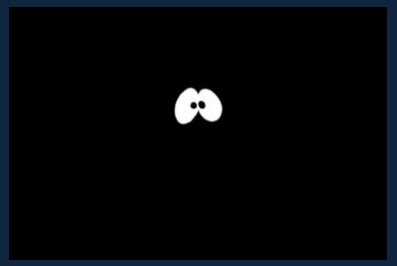
Not useful: urinary incontinence (Seizure: European Journal of Epilepsy, 2013-03-01, Volume 22, Issue 2, Pages 85-90) & “shaking”

Syncope

Autonomic (prodromal nausea and sweating)

- Problem with BP regulation
- No change in Life expectancy





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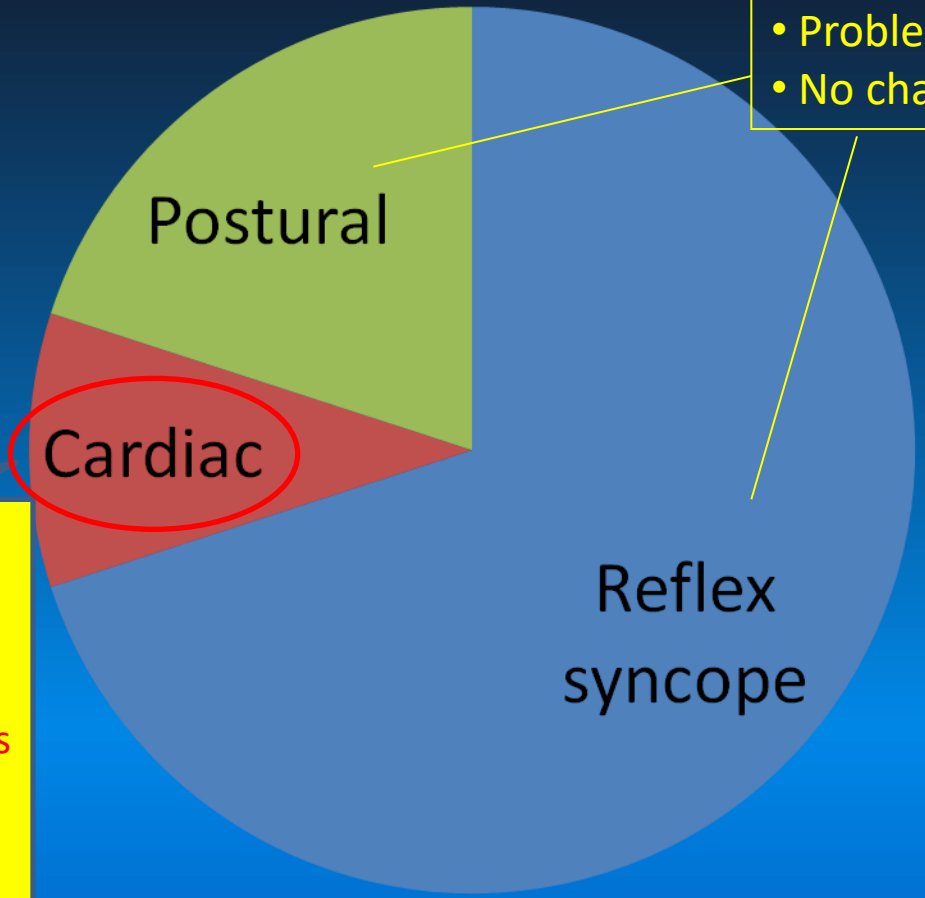


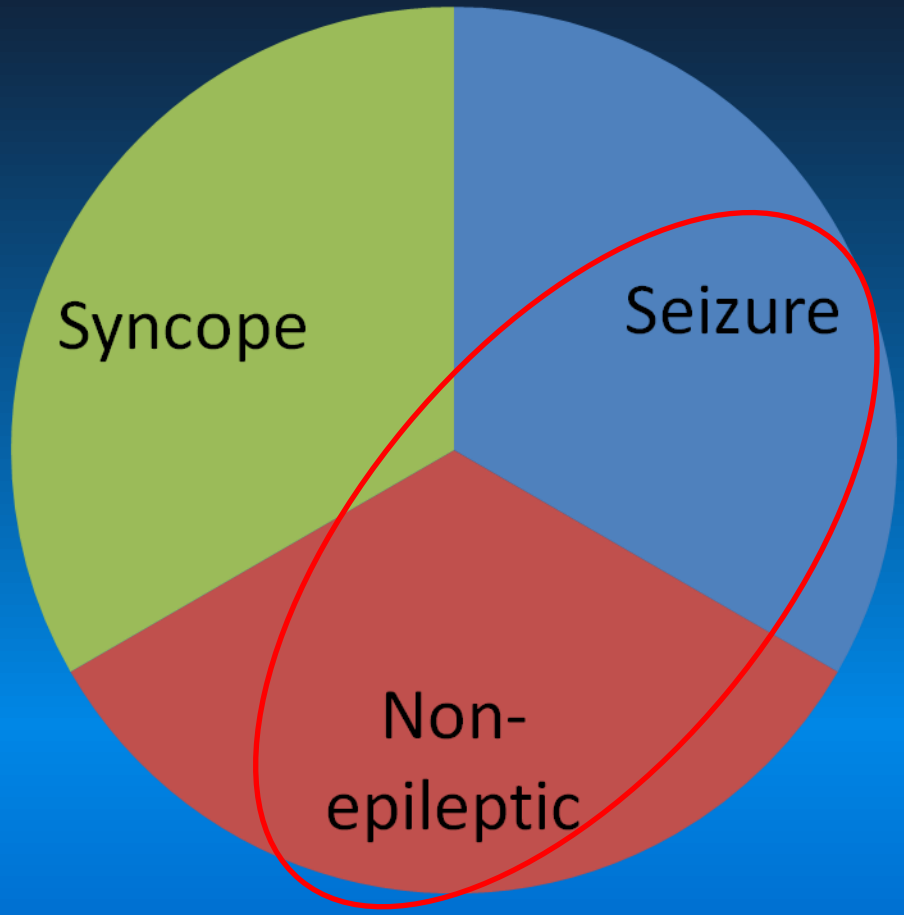
No trigger/abrupt

10%/yr risk of death

?FHx sudden death <35 yrs
?RF for IHD of PMH of IHD

ECG:
>35yrs: LBBB, Q-waves
<35yrs: Delta, PR, QT, LVH

Blackouts



Functional Neurological Disorder

Neurological Symptoms:

- Caused by a PROBLEM with the FUNCTIONING of the nervous system
- A “software” issue of the brain, not the hardware (as in stroke or MS)
- With positive diagnostic features typical of FND
- Cause day to day difficulties for the person who experiences them

(www.neurosymptoms.org)

Functional Neurological Disorder

Interoception:

- Decreased accuracy
- Increased self belief of accuracy

SPECT/fMRI:

- activation of emotional areas
- Deactivation of temporo-parietal areas in functional seizures (important for internal agency)

Non-epileptic attack

Psychogenic seizure

Functional seizures (FS)

Functional Non-epileptic attacks (FNEA)

Dissociative seizure

Pseudoseizure

TERMINOLOGY – PATIENT PERSPECTIVE

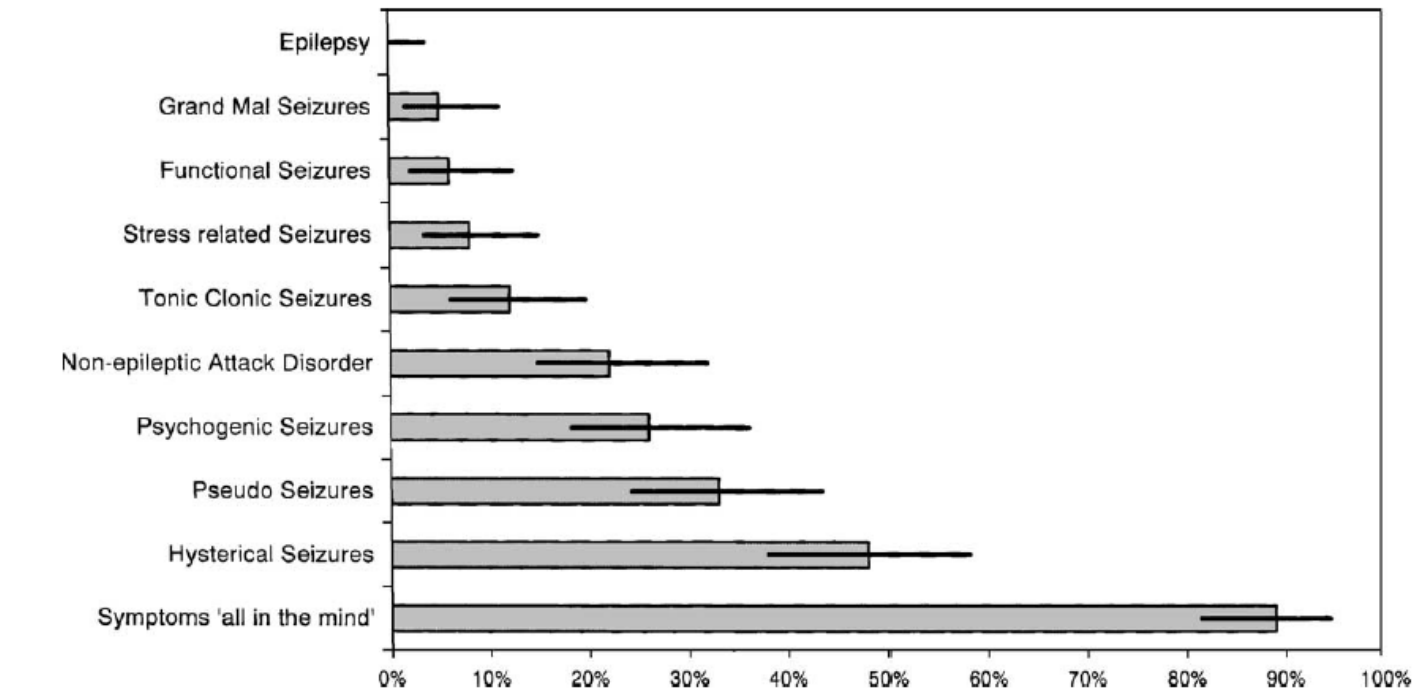


Fig. 1: Overall offensiveness of labels for blackouts—doctor would be suggesting I was 'putting it on', 'mad' or 'imagining symptoms' if I had blackouts and they gave me this diagnosis (%) (102 neurology patients). Bars represent 95% confidence intervals.

Stone et al, Seizure 2003; 12: 568–572

DUAL DIAGNOSIS OF FUNCTIONAL AND EPILEPTIC SEIZURES

- Functional seizures with additional epileptic seizures 22%
- Epileptic seizures with additional functional seizures 12%

Systematic review

M.A. Kutlubaev et al. / Epilepsy & Behavior 89 (2018) 70–78

Functional seizures (FS) vs Epileptic seizures (ES)

	FS	ES	Not helpful
Gradual onset			
Long duration			
Onset from sleep			
Asynchronous movements			
Pelvic thrusting			
Side-to side body/head movements			
Closed eyes			
Ictal Crying			
Opisthotonus			
Flailing or thrashing movements			
Tongue bite			
Urinary incontinence			
Memory recall			
Stertorous breathing			
Postictal confusion			

Avbersek; J Neurol Neurosurg Psychiatry 2010;81:719-725

Functional seizures (FS) vs Epileptic seizures (ES)

	FS	ES	Not helpful
Gradual onset			√
Long duration	√		
Onset from sleep			√
Asynchronous movements	√		
Pelvic thrusting	√		
Side-to side body/head movements	√		
Closed eyes	√		
Ictal Crying	√		
Opisthotonus			√
Flailing or thrashing movements			√
Tongue bite			√ (non-lateral)
Urinary incontinence			√
Memory recall	√		
Stertorous breathing		√	
Postictal confusion		√	

Avbersek; J Neurol Neurosurg Psychiatry 2010;81:719-725

Functional vs Epileptic seizures the importance of listening

Functional

- Metaphors of space/place patients go through
- Resistance to focusing on individual seizure episodes and only provide a detailed seizure description after repeated prompting
- Focussing on the impact on their lives

Epileptic

- Depicting the seizure as an agent/force or event/situation
- Volunteered detailed first person accounts of seizures

Plug et al. Seizure 18 (2009) 43–50

Schwabe et al, Social Sci & Medicine. Vol 65, Issue 4, Aug 2007, Pg 712-724

THE DIAGNOSTIC CODE

ILAE 2025 SEIZURE CLASSIFICATION

FOCAL

- Preserved consciousness
- Impaired consciousness

GENERALIZED

- Absence seizures
- Other generalised seizures

Focal to bilateral tonic-clonic

ILAE 2025 SEIZURE CLASSIFICATION

FOCAL

SPS – simple partial

Preserved consciousness

Impaired consciousness

CPS – complex partial

GENERALIZED

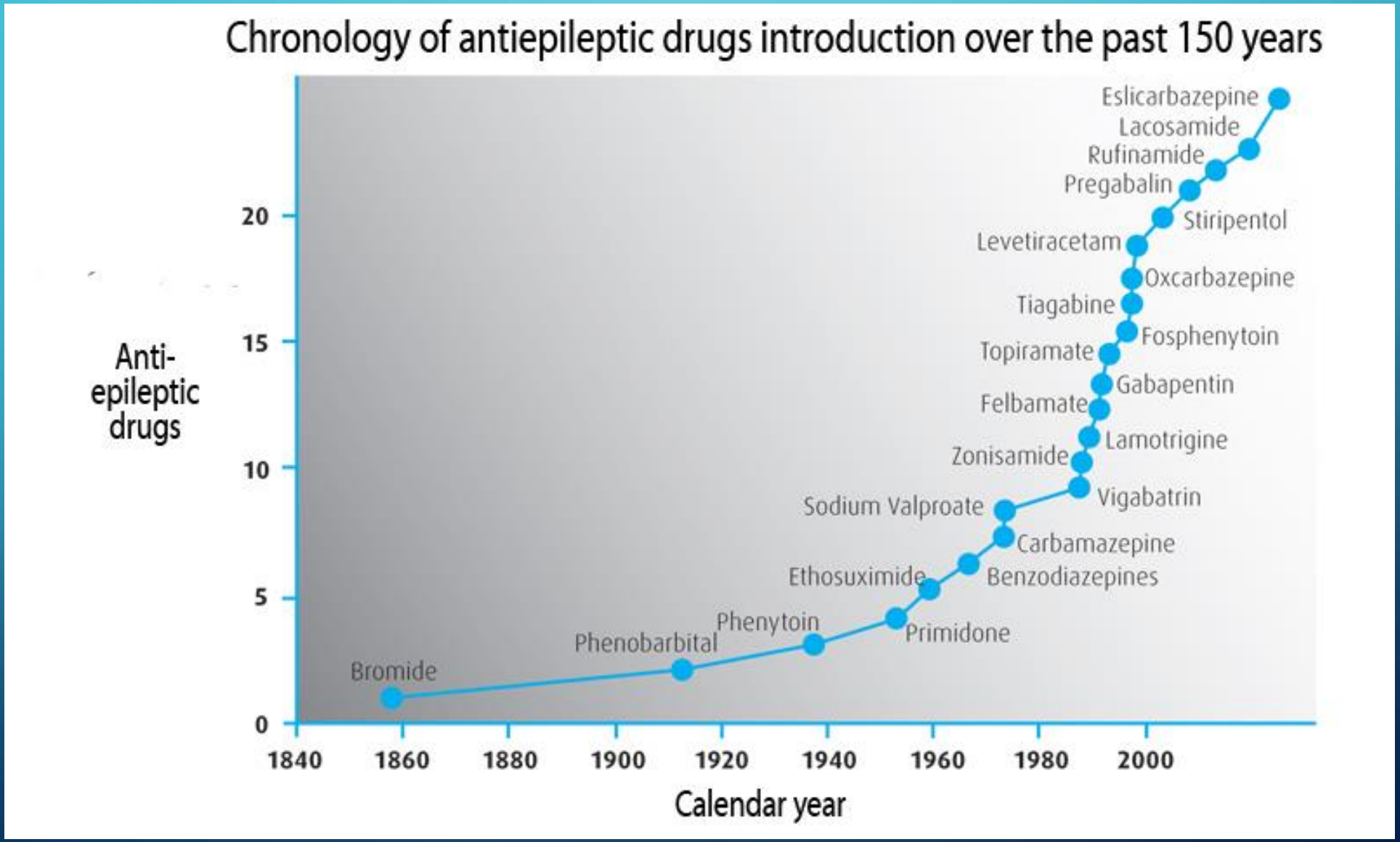
Absence seizures
Other generalised seizures

Focal to bilateral tonic-clonic

TREATMENT

TREATMENT

Cenobamate
Brivaracetam
Perampanel



Adapted copy from www.pmlive.com; original graph from Prof. Martin Brodie

ANTISEIZURE MEDICATION (ASM)– SOME SIDE EFFECTS

- Weight gain: Valproate, Gabapentin, Pregabalin
- Weight loss: Topiramate, Zonisamide
- Behaviour: Levetiracetam, Perampanel
- Depression: Levetiracetam, Zonisamide, Topiramate, Perampanel
- Memory: Topiramate, Zonisamide
- Renal calculi: Zonisamide, Topiramate

- Rash: Phenytoin 6%, Lamotrigine 5%, Carbamazepine 4%,

Enzyme inducers

Carbamazepine
Oxcarbazepine
Phenytoin
Phenobarbitone

Primidone
(Topiramate)

Bones ?

Antidepressants/
Antipsychotics ↓

Sex Hormones ↓
-> sexual dysfunction

Cardiovascular risk?

CANNABINOIDS

CBD
Cannabidiol

TCH
Tetrahydrocannabinol
<1%

- Epidiolex: ***Lennox-Gastaut & Dravet Syndrome***
- (Sativex for MS –> TCH:CBD 50:50)

- Potentiation of Clobazam and Valproate?

- ☠ NNH (number to harm): 8-22 ☠

- ☠ CBD-oils are unregulated! ☠

ASM – MONITORING

- Enzyme inducers: Vit B12, Folate, Calcium, Vit D, TSH (LFT, FBC, U&E)
- Yearly levels: Phenytoin & Phenobarbitone
- If concerns about toxicity: Carbamazepine, Phenytoin, Phenobarbitone
- Pregnancy: Lamotrigine, Levetiracetam, Carbamazepine
- Otherwise levels only if concerns about compliance

PROGNOSIS

PROGNOSIS

Seizure control: 50-60% with first ASM

Intractable: 10-20%

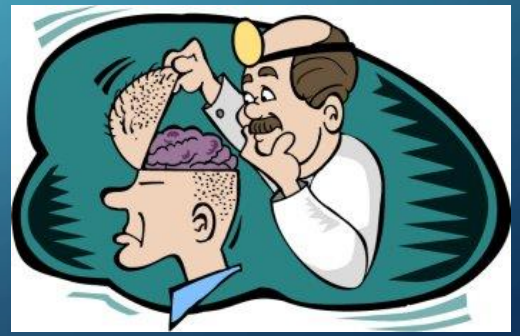
PROGNOSIS

Seizure control: 50-60% with first ASM

Intractable: 10-20%

- Surgery:
  - TLE: 50% Sz free + 20-30% Sz improvement
  - FLE: 30-40% Sz free

  - VNS (Vagal Nerve Stimulation)



ASM WITHDRAWAL

- Risk of seizure recurrence:
  - 2 yrs Sz free -> 20-40%
  - 5 yrs Sz free -> 10-20%

- Driving: stop from starting to wean until 6 months following cessation

SUDEP
(SUDDEN UNEXPECTED DEATH IN EPILEPSY)

- 1% if frequent GTCS
- 0.5% overall

- Risk factors:
  - GTCS frequency
  - Nocturnal seizures

CO-MORBIDITIES

- 2-3x higher mortality (even if Seizures are controlled)

- Depression
- Anxiety
- Substance misuse

Epilepsy and Woman

- OCP -> beware with enzyme inducers
  (CBZ, OXC, PHT, TOP, Phenobarbitone, Primidone)

Alternatives:

- DMPA, progestogen-only injectable
- Cu-IUD, copper intrauterine device
- LNG-IUS, levonorgestrel-releasing intrauterine system

Lamotrigine and OCP

- Oestrogen-OCP reduces Lamotrigine level !!!!
  - Potential loss of seizure control
- Desogestrel might increase Lamotrigine levels (not others)
- ?Lamotrigine reduces progesterone?

FSRH guidance

ASM and Pregnancy

- Lamotrigine and Levetiracetam are safe
  - (risk same as baseline, e.g. 2-3%)

- Unsafe:
  - Carbamazepine (4-5%)
  - Topiramate (4-5%)
  - Phenytoin (6%)
  - Phenobarbital (6-7%)
  - Valproate (10%)

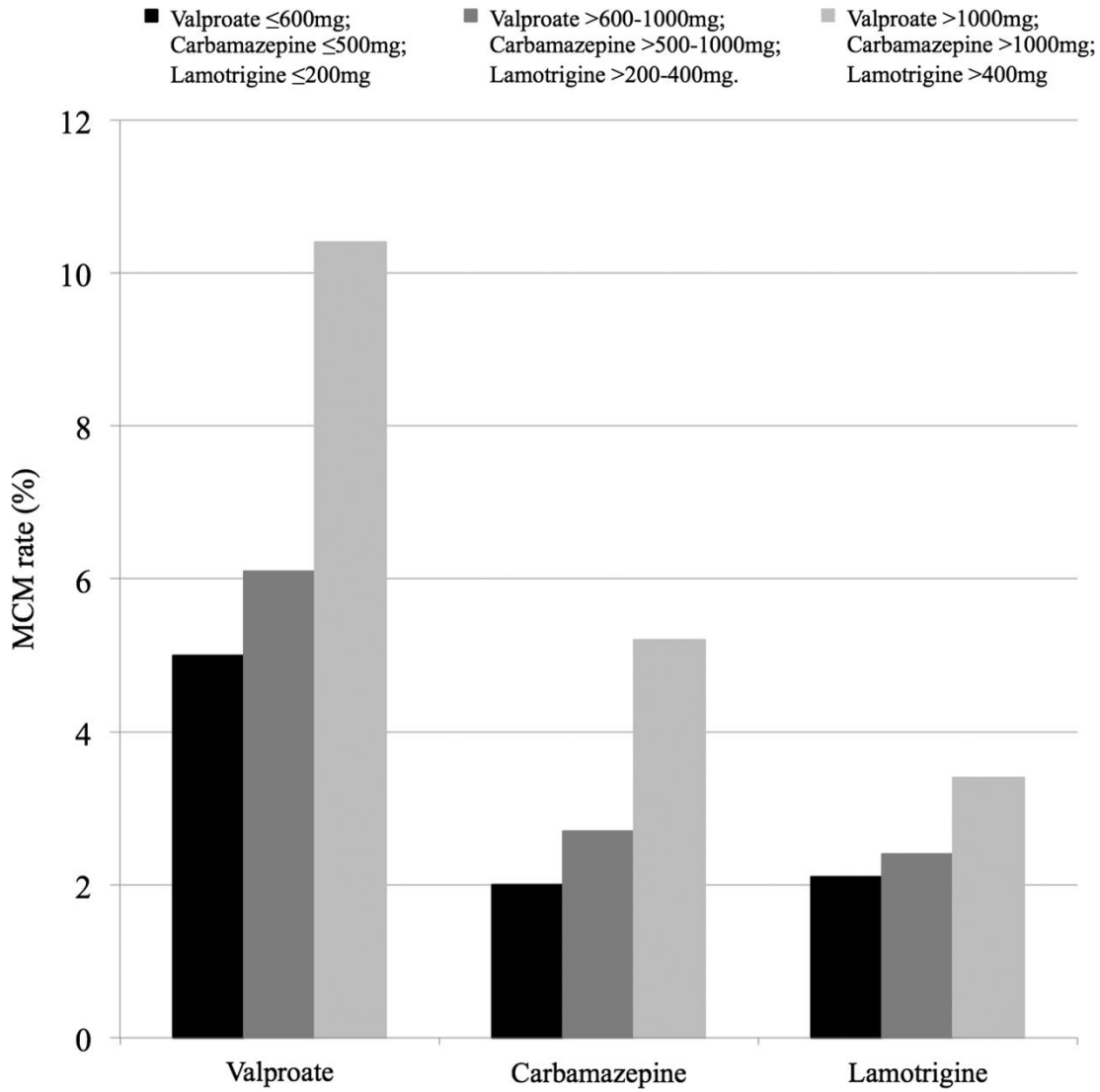
Potential increased risk:
- Pregabalin
- Gabapentin
- Clobazam

More data needed:
- Zonisamide (small growth?)
- Clonazepam (safe?)

All others – insufficient data

MHRA 2021

ASM and Pregnancy



J Neurol Neurosurg Psychiatry 2014;85:1029–1034

Valproate & Women

- **Foetal malformation risk: 10%**
- **Developmental problems in newborn 30-40%**
- **Increase in autism**

- **Annual Valproate Risk Form (by specialist)**
  - **+ 1x second specialist signature**
- **Pregnancy prevention program (contraception: coil, implant; other + barrier)**

Valproate & Men

- Valproate may cause infertility in men, that may be reversible after treatment is stopped or the dose is reduced in some patients.
- A study of health records reported that around 5 in 100 children whose fathers were taking valproate at conception had a developmental disorder. This was compared to around 3 in 100 children whose fathers were taking lamotrigine or levetiracetam: two other anti-seizure epilepsy medicines. The study did not look at risks for children whose fathers did not take any medication. Whilst this study doesn't prove that valproate use in men increased the risk of problems in children, it is an important safety concern that warrants action on a precautionary basis.

Valproate Risk Form x2 signatures (new starters only)

Topiramate

☠
Congenital malformations,
Neurodevelopmental disorders,
Fetal growth
☠

Highly effective contraception - preferably

a) copper intrauterine device (Cu-IUD)
b) levonorgestrel intrauterine system (LNG-IUS)
c) or two complementary forms of contraception including a barrier method

Needs specialist – yearly

Can be on Topiramate in pregnancy
– but try to change or at least lower the dose

Step 2: Explain the risks to the patient and document awareness

Specialist prescribers and patients (or responsible persons) must both complete this section of the form. This records that you have discussed the risks of taking topiramate during pregnancy and the measures needed to reduce the risks. The patient (or responsible person) must also sign the form to confirm they are aware of these risks.

Information to be discussed with the patient	Specialist Prescriber to initial to confirm you have discussed	Patient (responsible person) to initial to confirm you are aware
Their medication should be reviewed regularly (at least once a year). At this review, your specialist prescriber will decide with you whether topiramate continues to be the best treatment for you. This will take into account any change in your circumstances.		
Topiramate can cause serious harm to an unborn baby if taken by a mother during pregnancy. For babies of mothers who take topiramate while pregnant the risks are: • Around 4 to 9 babies in every 100 will have birth defects, this compares with 1 to 3 babies in every 100 born to mothers in the general population. • A 2-3 times higher risk of autism spectrum disorder, attention deficit hyperactivity disorder and intellectual disabilities compared with women without epilepsy not taking epilepsy medicines. • Around 18 in 100 babies will be born small for gestational age; this compares with around 5 in 100 babies of mothers in the general population.		
Need for a pregnancy test to exclude pregnancy before starting topiramate. Further pregnancy tests may be needed during treatment.		
Need to use effective birth control (contraception) at all times while taking topiramate and for four weeks after stopping topiramate.		
The importance of contacting their GP for referral to the specialist as soon as they are thinking about becoming pregnant. This is to make sure that there is time to switch to another treatment before the child is conceived and before birth control (contraception) is stopped.		
The need to contact their GP immediately, to be referred to the specialist for an urgent review of their treatment, if they think they may be pregnant.		
Risks of stopping topiramate for epilepsy without medical advice. They should not stop taking topiramate or change their dose unless they are told to do so by their specialist. This is because their condition may become worse, including an increase in seizures.		
A copy of the Patient Guide has been offered		
Signature of Specialist Prescriber:	**Date**	
Name of patient:		
Name of responsible person (if applicable):		
Signature of Patient (or responsible person, if applicable)	**Date:**	

MHRA approval date: 31 May 2024

ASM and breast feeding

- Generally safe !!
- Possible benefit of breast feeding for baby
- Caution with: Benzodiazepines, Primidone, Phenobarbitone -> can make drowsy
- Monitor: Lamotrigine (rash, drowsy)

G. Veiby et al. Seizure 28 (2015) 57–65