

→ Anna Hess's note

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## SEIZURES

### Epilepsy:

Prominent Alteration of behaviour due to disordered synchronous and Rhythmic firing of population of brain neurons.

### EPILEPSY:

Disorder of brain function characterized by periodic and unpredictable occurrence of seizures.

### CLASSIFICATION

→ focal  
→ generalized  
→ onset (unknown)

### FOCAL ONSET SEIZURES:

- Unilateral origin
- Focal Awareness : no loss of con
- Focal Impaired Awareness : loss of con

### GENERALISED

- Diffused origin
- GTCS (generalized tonic clonic seizures)
- Absence (previously petit-mal).
- Myoclonic
- Atonic
- Dravet syndrome of infancy → severe epilepsy

## Patho Physiology

- Seizure due to Abnormal depolarisation of neuronal membrane → hyperexcitability of high frequency firing.
- An imbalance or defect in Na, Ca, K or Cl ion conductance across membrane
- Defect in inhibitory GABA
- Excess of excitatory neurotransmitter like Glutamate (NMDA & AMPA Receptors)

↓ electrolyte imbalance ↓ GABA ↓ Glutamate

## Antiepileptic drugs: CLASSIFICATION:

- Barbiturates: Phenobarbitone
- Deoxybarbiturates: Primidone
- Hydantoins: Phenytoin, Fosphenytoin
- Imidazolidines: Carbamazepine
- Oxazepamine: Ethosuximide
- Succinimide: Ethosuximide
- Amino acid analogues: Valproic Acid
- Benzodiazepines: Diazepam, Lorazepam
- Phenyltriazines (lamotrigine): SILENOR
- Cyclic GABA Analogue: Gabapentin, Pregabalin

• Neurol drugs - Topiramate, Zonisamide

Tiagabine, Vigabatrin, Levetiracetam.

Rufinamide, Ethosuximide,

Lacosamide, Brivaracetam.

### CLASSIFICATION BASED ON MOA

1) Inhibition of voltage gated  $Na^+$  channel

- Block  $Na^+$  channel that cause repetitive neuronal firing.

- Bind to and prolong the duration of inactivated phase of delayed Reversion to Resting phase.

Drugs - Phenytoin

Sodium Valproate

Carbamazepine

Lamotrigine

Topiramate

Zonisamide

Lacosamide.

2) Enhancement of GABAergic Action

• Some AEDs Activate GABA A Receptor to

facilitate GABA mediated Cl channel opening

- RZP, Baclofen

• GABA Transaminase, (Metabolize GABA to inhibit)

- Vigabatrin

• GABA Uptake transporter (GAT) Inhibition

Tiagabine, Valproate

3) Blockade of NMDA/AMPA Receptor Glutamate Receptor

→ seizures

1) Glutamate Receptor blockers - Rufinamide

2) NMDA Blocker → Felbamate

3) AMPA Blocker: Perampanel, Lamotrigine, Topiramate

4) Blockade of Na<sup>+</sup>-V type Ca channels.

Reduce glutamate Release - lamotrigine  
cetyphenin.

5) Blockade of T type Ca channels.

Responsible for Absence seizures.

\* Ethosuximide, Valproate

6) Selective blocking to synaptic vesicular proteins

(SV2A)

• Reduce synaptic Release of glutamate

• ↑ synaptic Release of GABA

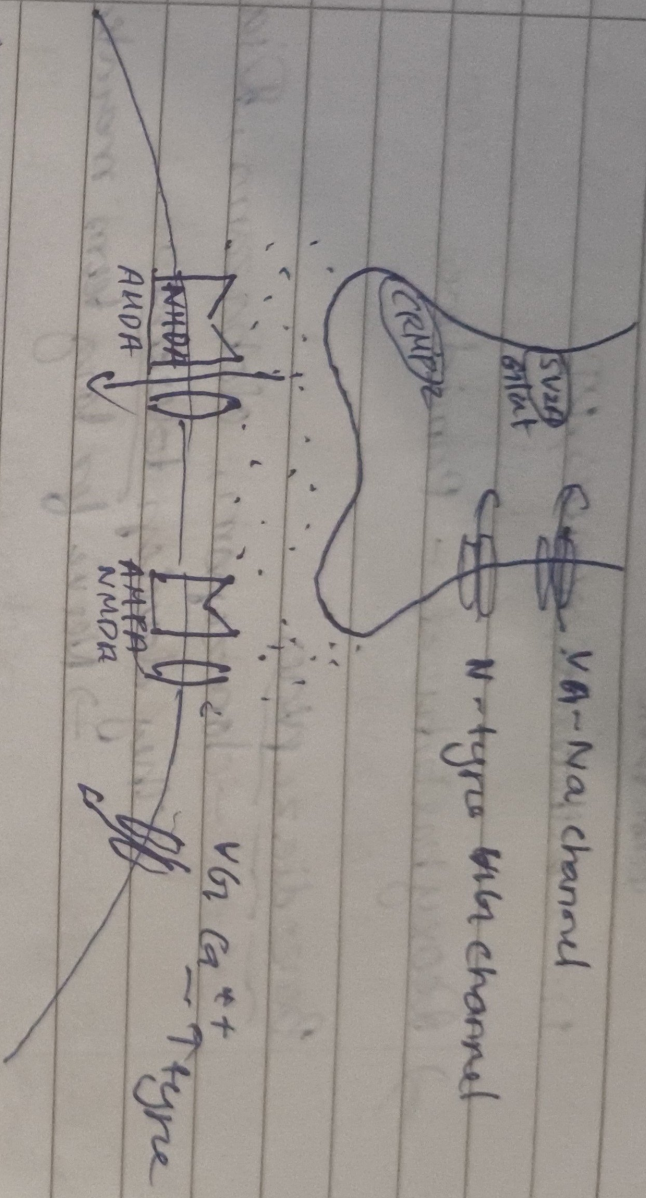
- levamisole, Brivaracetam

7) Blockade of CRMP-2 (blocking Response mediator protein 1 input) for Release of

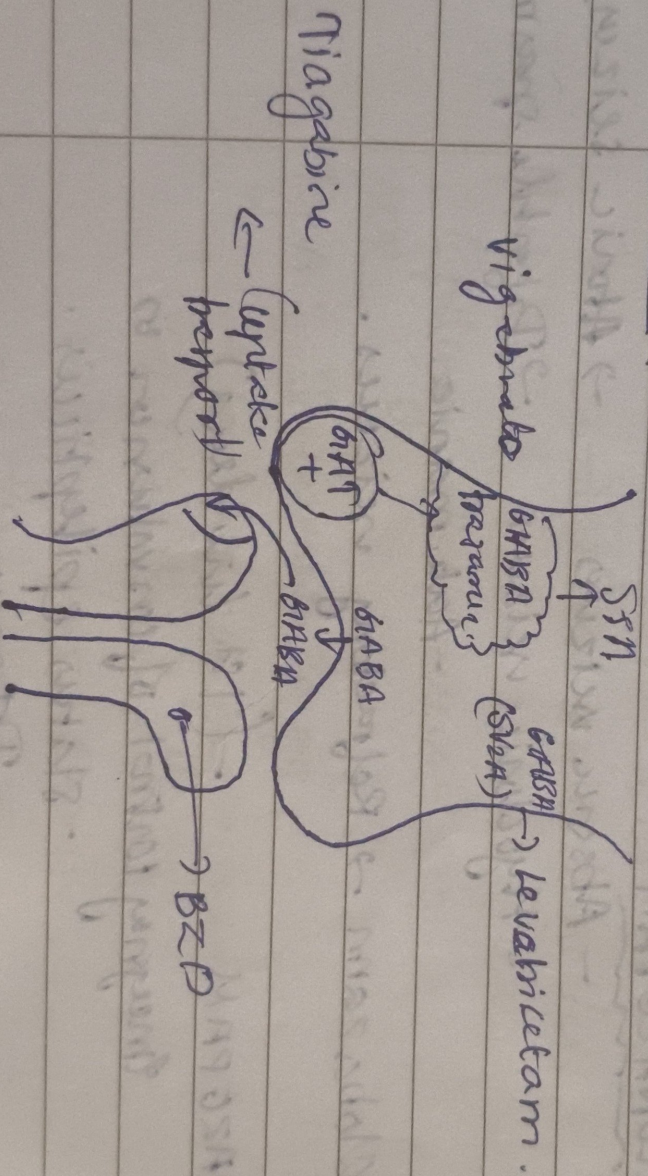
epilepticogenic factors.

- levetiracetam

Glutamate



GABA



2)

Barbiturate - Anesthetics:

Anticonvulsant Action → No given.

No tolerance.

Uses: → GTCs, Basal Seizures, status epilepticus.  
Prophylaxis of periodic seizures.

Ad → cheapest.  
least toxic.

Dis → withdrawal seizures, DT

→ Doxybabituxol - Primidone

Benzodiazepines

→ clonazepam, clobazam, Diazepam

→ They develop tolerance

→ Need for long term maintenance

CLONAZEPAM

- Absence seizures

→ Atonic seizures

- Myoclonic seizures

→ Partial spasms

- Acute mania.

Clobazam → Refractory seizures.

# DIAZEPAM

- (1<sup>st</sup> line drug)

Emergency control of convulsions is

• Status epilepticus.

• Tetanus.

• Eclampsia

• Febrile seizures: (Rectal)

Disadvantage:

- Sedation

- Rapid tolerance

→ The metabolites of injected vein.

→ Marked fall of B.P., Resp

## # Lorazepam:

1<sup>st</sup> choice - for status epilepticus.

Dose - 0.1 mg/kg IV

LORAZEPAM - less thrombophlebitis & more sustained Action

Hydantoin - Phenytoin, Fosphenytoin.

Older, non-selective AED

MOA  $\rightarrow$  Inhibit Na channel - Prolong Discharge  
PK  $\rightarrow$  slowest Absorption. (Phen)

Metabolised in liver (CYP2C9/1A)

$\rightarrow$  Mixed order kinetics.

Uses:

Epilepsy, Focal seizure

AED.

TyxA: In the epinephrine range

$\rightarrow$  Gum hyperplasia - overgrowth of connective tissues.

$\rightarrow$  Hirsutism, acne.

$\rightarrow$  Megaloblastic anemia.

$\rightarrow$  Osteomalacia.

TyxB: Hypersensitive Rx (rash, DLE, lymphadenopathy).

Teratogenicity - Fetal hydantoin syndrome.

$\hookrightarrow$  cleft lip & palate.

Microcephaly, HI syndrome, pharyngeal

Higher dose level

cerebellar and vestibular manifestation  
N/V, TV  $\rightarrow$  bilateral damage  
(hypotension, asysthymia, monitoring)

• Potent enzyme inducer of CYP2C8/9

CYP3A4/5

• Inhibits CYP2C9/19.

~~Phosphorylation~~

$\Rightarrow$  Carbamazepine  $\rightarrow$  chemically related to  
Trimipramine (TCAs)

MOA: Inhibits VGNa channels,

$\uparrow$  GABA

PK  $\rightarrow$  Good oral absorption

90% PPB

U<sub>ref</sub>: Epilepsy - Broad spectrum

DOC in Absence seizures

CAWS

ADR

$\rightarrow$  BRS/S

CR/E

$\rightarrow$  weight gain

$\rightarrow$  Ataxia

$\rightarrow$  Carboxy of vari

Plasma

Ataxia/seizures

Fatal if food to BRS

Hypotension/seizures

Mania, bipolar, paroxysmal

Migraine prophylaxis

Adverse toxicity

4A

Teratogenicity.

- Neural tube defect
- spina bifida.

Divalproex:

→ coordination complex (valproic acid and sodium valproate (1:1))

→ Better gastric tolerance  
Ethosuximide

— Block V or T-type Ca channel

Uses

DOC → Absence of seizure.

Newer AEDs:

→ Drug developed after 1990. → expensive.

→ Multiple targets of action → very effective

→ Broad spectrum → expensive

→ Equally effective

Sedation, tremor, rash.

Levetiracetam CPD below 14

→ febrile convulsion

→ sparing.

1st choice  
2nd choice  
3rd choice  
4th choice  
5th choice  
6th choice  
7th choice  
8th choice  
9th choice  
10th choice

1st choice

2nd choice

3rd choice

4th choice

5th choice

6th choice

7th choice

8th choice

9th choice

10th choice

Report once after 10min if needed

1st choice of 6

2nd choice

3rd choice

4th choice

5th choice

6th choice

7th choice

8th choice

9th choice

10th choice

11th choice

12th choice

13th choice