Screening Method Of Anti-Epileptic

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Introduction

- Epilepsy is a very commaon disorder characterised by seizures, which take various forms and result from neurongal discharges, with or without characteristic body movement.
- Epilepsy derived from Greek - epilepsia - “taking hold of”
- Characterized by two or more unprovoked seizures.
- Epilepsy was described by JH Jackson.

Symptom

- Seizure symptoms vary depending on the type of seizure. Because epilepsy is caused by certain activity in the brain, seizures can affect any brain process. Seizure symptoms may include:
- Temporary confusion.
- A staring spell.
- Stiff muscles.
- Uncontrollable jerking movements of the arms and legs.
- Loss of consciousness or awareness.
- Psychological symptoms such as fear, anxiety

Classification of Seizures

Primary Genralised

Tonic-Clonic seizure

Absence seizure

Atonic seizure

Myoclonic seizure

Partial Seizure

Simple partial seizure

Complex partial seizure

Partial seizure

Unclassifed Seizure

Infantile spasms

Generalised seizure

- Whole brain invoved
- Characterised by immediate loss of consicousness
- Type of genralised seizure

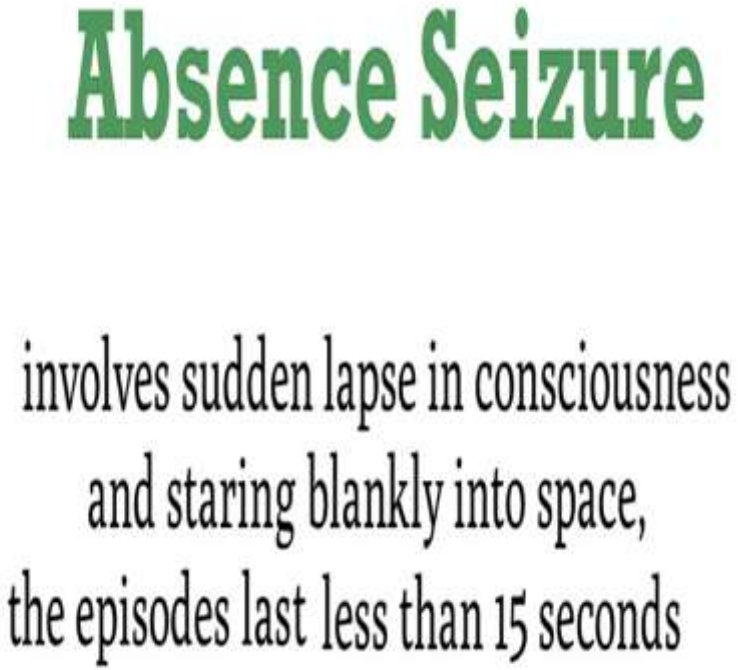
1.Tonic-clonic seizure(grand mal epilepsy):-

Cry - Unconsciousness - strong contraction of all body muscles - clonic jerking - prolonged sleep

1-2 min

Absence Seizure(Petit Mal Epilepsy)

- Prevalant in childern.
- Momemtary loss of consciousnees
- Patient freezes & stares in one direction
- No muscular movement & jerking
- 1/2 mins

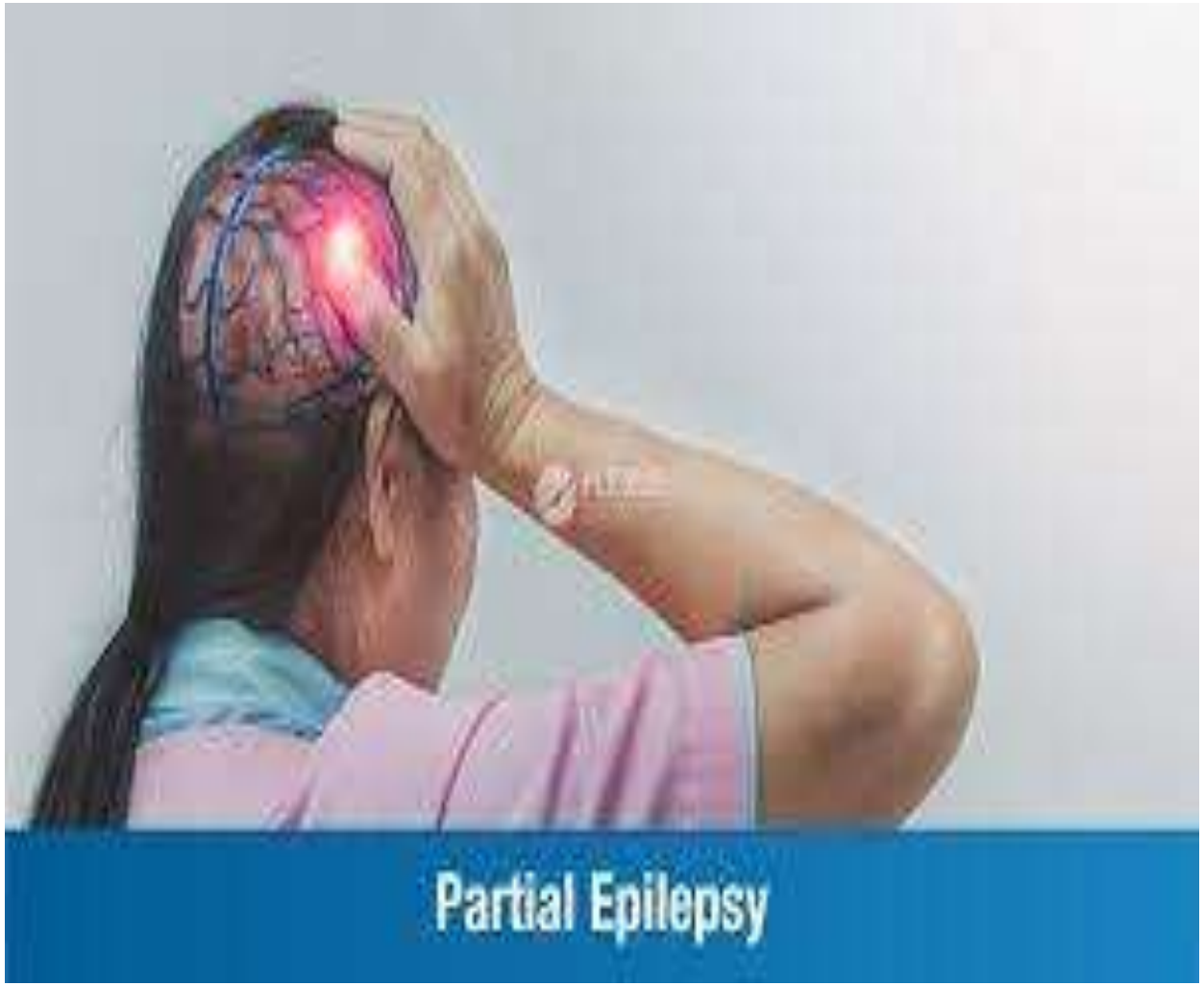


Atonic seizure

- Due to excessive inhabitory discharge
- Relaxation & patient fall.
- Atonic seizures are a type of seizure that causes sudden loss of muscle strength. These seizures are also called akinetic seizures, drop attacks or drop seizures.

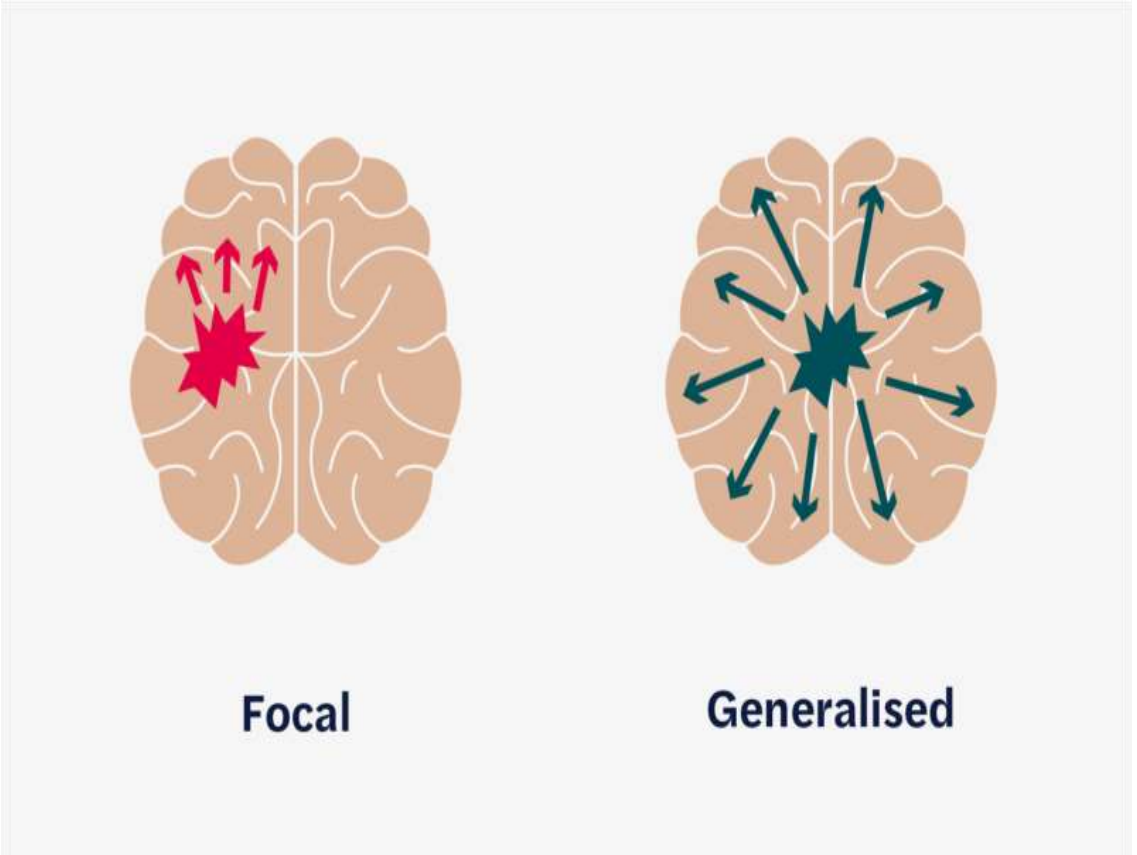
Partial Seizure

- Discharge begins locally, remain localised.
- Symptoms depend on the brain egion involved.
- Also known as Psychomotor epilepsy.



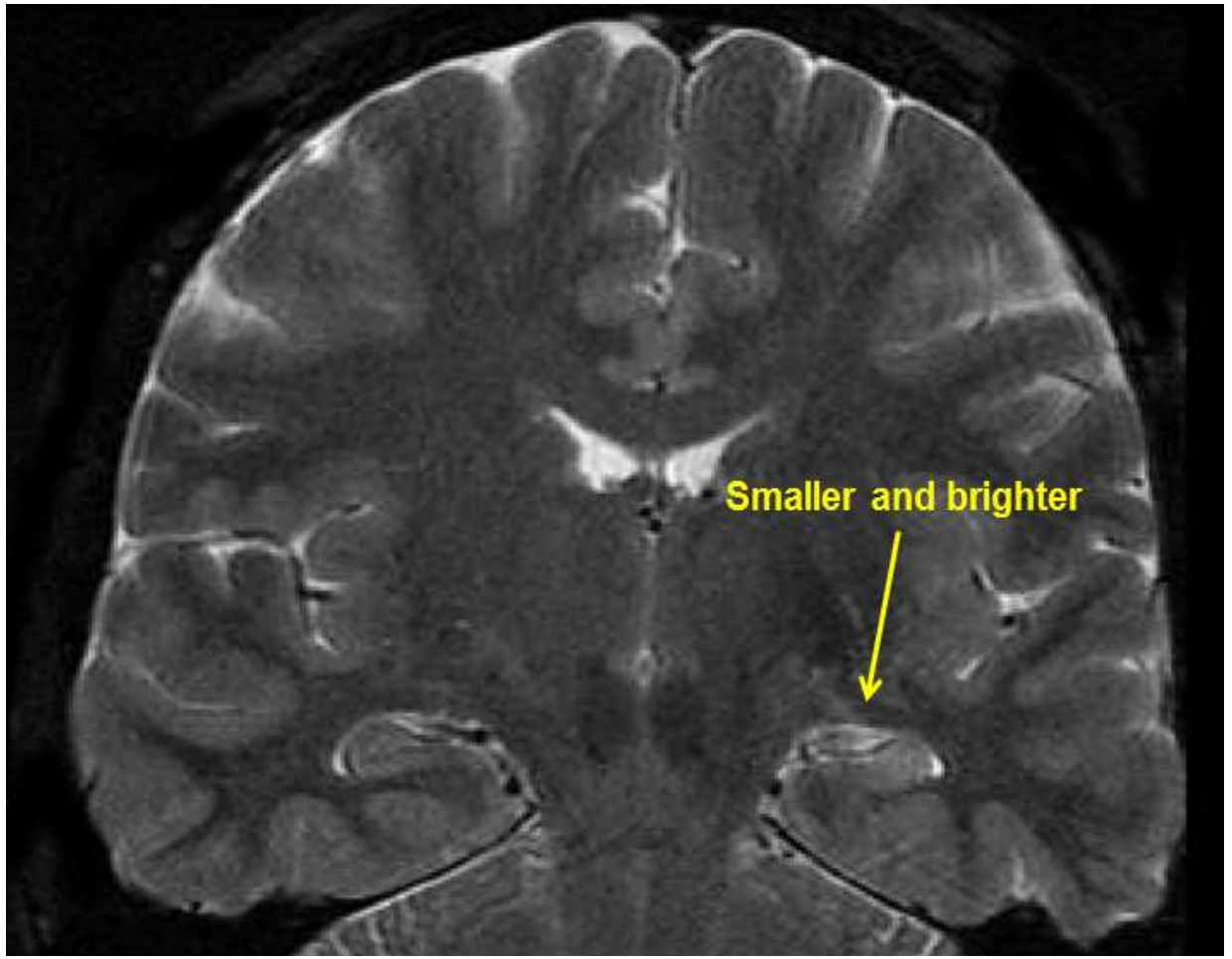
Simple partial seizure (Focal epilepsy)

- Involvement of area of cotex causes convulsions.
- No loss of consciousness.
- 1/2 to 1 min.
- Focal seizures are a type of seizure that affects only one side of your brain and body



Complex partial seizure

- Attack of bizarre purposeless movement.
- Impairment of consciousness.
- 1-2 min.



Pathophysiology Of Epilepsy

- Seizures develop due to an imbalance between inhibitory and excitatory signals in the brain.

- A seizure may initiate due to high-frequency bursts of excitatory action potentials in neurons. This leads to synchronous, hyperexcitable activity within a neuronal population.

- In epilepsy, acquired or genetic factors effect the balance between inhibitory (i.e. gabanergic) and excitatory (i.e. glutamatergic) signals.
- Gabanergic: inhibitory, characterised by gamma-aminobutyric acid (GABA) receptors. Ligand-gated ion channel that allows flow of chloride ions. GABA is the main inhibitory neurotransmitter that binds to these receptors.
- Glutamatergic: excitatory, characterised by glutamate receptors (multiple types: ion-channels and G-coupled protein). Glutamate is a small neurotransmitter that can active these receptors.

Selection of Anti-epileptic Drug

Primary GTC	Partial	Absence	Atypical,Myoclonic
Valpraote	Carbamazepine	Valpraote	Valporate
Lamotrigine	Phenytoin	Ethosuximide	Toprimate
Toprimate	Valpraote		

PRECLINICAL EVALUATION

Animal Models of Seizure

- The usual approach to anticonvulsant drug testing in animal is to observe effect of prior drug administration on seizure produced by
- 1. Electrical stimulation of brain
- 2. Systemic adminidtration of a convulsant drug
- 3. Animal strains with spontaneous or sensory-evoked convulsions

In Vitro methods

- Hippocampal slices
- Electrical recording from isolated brain cells
- GABA uptake in rat cerebral cotex
- TBPS binding assay

Method(in vivo method)

- Electroshock seizure

  1.Pentylenetetrazol(PTZ) induced seizure

  2.Thershold models

  3.Strychine-induced convulsions

  4.Isoniazid-induced convulsions

Theshold Models

Aim- Used to screen drug with efficacy against generalized tonic clonic and focal seizure.

Requriment- Animal required- Mice (18-30gm)

Equipment required- Electrical Stimulator

Procedure- Animal section

Experimental grouping(Divided in to animal in to different group)

Acclimation

Baseline measurement(Record under study before any interventions)

Intervetion

Data collection

Threshold model(analyze the critical point)

Report and publication

Pentyleneterazole Induce Convulsion

Aim- To evaluate antiepileptic drugs. Pentylenetetrazole is a CNS Stimulant. It produces jerky type of clonic convulsion in rats and mice similar to petit mal type of convulsion in man.

It causes direct depolarization of central neuron.

Also interfere with GABAergic inhibition.

Procedure- Two group of 10 Albino Swiss mice of either sex (20-25gm).

- First group is injected with Diazepam 4mg/kg(i.p.).

- Second group as control.
- 30min after Diazepam treatment inject with 75 mg/kg of PTZ by s.c.
- Each animal is observed for 1hr. in plastic cage.
- Seizure & myclonic convulsion are recorded.
- At least 80% of animal in control have to show convulsion.

Evaluation- The number of protected animal in treated group is calculated as percentage of affected animal in control group.

- ED 50 value calculated & time interval between PTZ injection and occurance of seizure can be meaured.

Isoniazid Induce Convulsion

Aim- Isoniazid is regarded as GABA synthesis inhibitor. it is known to purpose convulsion in patient having history of seizure.

Procedure- Two group each of 10 albino mice (18-22gm)

- First group is injected with Diazepam 5mg/kg(i.p.)
- Second group as control receive vehicle saline 10ml/kg
- 15min after s.c. injection/30 min after i.p./60 min after oral route 300 mg/kg of INH injected by s.c. to the both group.
- During next 120 min clonic seizure tonic seizure and death is recorded.

- At leat 80% of animal in control have to show convlsion.

Evaluation:-

- The percentage of seizure or death occuring in the control group is taken as 100%.
- The supression of these effects in the treated groups is calculated as percentage of control.ED 50 values are calculated.