NEUROPSYCHIATRIC ASPECTS OF EPILEPSY

Outline

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- Mechanism
- Classification
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- Anatomically defined epilepsy
- Neurodiagnostic test
- Management

Definition

An intermittent stereotyped disturbance of consciousness behaviour emotion motor function or sensation that on clinical grounds is believed to result from cortical neuronal discharge

Chadwick 1994

Terms associated with seizures

- Ictus The seizure itself
- Inter ictal period The period between post ictal abnormalities and the next ictus
- The Peri ictal period Period just before or after the ictus This term is applied when there is insufficient information to know when the ictus ends or begins

History

- Hippocrates 460 to 377BC attacked the prevailing belief that those afflicted with epilepsy were possessed by gods or goddesses
- He proposed that epilepsy was a brain disease caused by the blockage by phlegm of air carrying vessels to the brain
- In the 18th century the first so called scientific treatise on epilepsy since ancient times attributed seizures to masturbation

History

- Bromides which were introduced to diminish libido and masturbation proved to be the first successful antiepileptic medication
- With the development of effective antiepileptic drugs and the introduction of EEG physicians have come full circle to Hippocrates' belief that epilepsy is rooted in organic brain disease

Mechanism of Epilepsy

Abnormal electrical discharges are due to hyper excitable neurons with sustained postsynaptic depolarization

- Proposed mechanisms for this sustained depolarization include changes in ionic conductance decreased γ aminobutyric acid GABA inhibition of cortical excitability and increased glutamate mediated cortical excitation result in abnormal neuronal firing
- Anti epileptic drugs reduce this abnormal firing through blockade of calcium channels

Classification of Seizures

2010 ILAE Classification of Epileptic Seizures

1. Focal onset seizures
2. Generalized onset seizures
3. Seizures with unclear mode of onset
4. Epileptic spasms

ILAE 2017 Classification of Seizure Types Expanded Version

Focal Onset

Aware | Impaired Awareness

Motor Onset
- automatisms
- atonic
- clonic
- epileptic spasms
- hyperkinetic
- myoclonic
- tonic

Non-Motor Onset
- autonomic
- behavior arrest
- cognitive
- emotional
- sensory

focal to bilateral tonic-clonic

Generalized Onset

Motor
- tonic-clonic
- clonic
- tonic
- myoclonic
- myoclonic-tonic-clonic
- myoclonic-atonic
- atonic
- epileptic spasms

Non-Motor (absence)
- typical
- atypical
- myoclonic
- eyelid myoclonia

Unknown Onset

Motor
- tonic-clonic
- epileptic spasms

Non-Motor
- behavior arrest

Unclassified

- FOCAL SEIZURE previously called partial seizures these start in area or network of cell on one side of brain
- GENERALIZED SEIZURE previously called primary generalized these engage or involved network on both side of the brain at the onset
- UNKNOWN ONSET if the onset of seizure is not known the seizure falls into the unknown onset category Later on the seizure falls false into the unknown category
- FOCAL TO BILATERAL SEIZURE starts in one side or part of brain and spreads to both sides has been called a secondary generalized seizure

Psychopathology in Patients with Seizure disorders

- 20 to 60 percent prevalence of psychiatric problems among epilepsy patients
- Epilepsy patients are prone to psychosis mood disorder especially depression anxiety disorder somatic symptom disorders personality disorders hypo sexuality and dissociative symptoms
- These problems are approximately equally divided between those that occur ictally or peri ictally and those that occur interictally or are variably related to the ictus

Psychopathology

- The pattern of behavioural changes in seizure patients appear specific to epilepsy
- On the Minnesota Multiphasic Personality Inventory MMPI 2 patients with epilepsy have higher schizophrenia scale and paranoia scale scores than patients with other neurological disabilities
- Psychiatric disturbances primarily psychosis and personality disorders more common in patients with focal onset seizures compared to those with generalized tonic clonic seizures

Psychopathology

- Major depression dissociative symptoms obsession and compulsion were also seen more frequently in temporal lobe epilepsy compared to generalized epilepsy
- 60 to 70 percent of adults with epilepsy regardless of seizure type have a temporal lobe focus and many generalized tonic clonic seizures are secondarily generalized from temporal lobe focus without a preceding focal dyscognitive seizure
- Psychic auras from the temporal lobe particularly if associated with negative feelings eg jamais vu and fear predispose to psychosis or personality disorders

Psychic Auras

Type	Symptoms	Probable Source
Dysphasic	Nonfluent Impaired comprehension	Left perisylvian language areas
Dysmnesic	*Déjà vu, déjà vécu, déjà pensé, déjà entendu, jamais vu*, etc., prescience, illusion of memory	Mesobasal temporal, especially on right
Cognitive	Dreamy state, altered time sense, derealization, depersonalization	Mesobasal temporal and temporal neocortex
	Forced thinking, forced actions, and altered or obscure thoughts	Frontal association cortex
Affective	Fear, anxiety, apprehension, depression, pleasure, displeasure	Mesobasal temporal and temporal neocortex
Illusions	Macropsia, micropsia, teleopsia, metamorphopsia, increased color intensity, increased stereopsis intensity	Lateral superior temporal neocortex, especially on right for visual illusions
Hallucinations	Structured, hallucinatory remembrances, autoscopy	Mesobasal temporal and temporal neocortex

Psychopathology

- The relationship of seizures psychiatric syndromes and the mediobasaltemporal lobes implies that many behavioural changes are more than psychological reactions to the psychosocial stressors of epilepsy
- Temporal limbic stimulation evokes psychic auras and automatisms
- Amygdala stimulation results in aggression
- It was also found that repeated application of epileptic agents to induce behavioural changes Kindling on limbic structures caused psychotic behaviour in cats

Psychopathology

There are also several potential organic causes of psychiatric disturbances in epilepsy such as

- Genetic or developmental disturbances
- Changes in spike frequency altered receptor sensitivity kindling
- Absence of function at the seizure focus Inhibition hypo metabolism dysfunction or downregulation of affected areas
- Neurochemical causes which involve dopamine and other neurotransmitters and endorphins
- Gonadotropins and other endocrine hormones
- Sleep disturbances

Behavioural disorders in Epilepsy

- Psychiatric behaviours associated with epilepsy can be categorized with their relationship to the ictus or seizure discharges
- These can be a part of ictus peri ictally or during the inter ictal period

Ictal Features

- Seizure discharges can produce semi purposeful automatisms and psychic auras such as mood changes derealisation and depersonalization and forced thinking
- There may be ictal fear and ictal depression which can extend up to days or months after seizure has passed
- Some patients have pleasurable auras Fyodor Dostoyevsky had "ecstatic aura for a few seconds of such bliss"
- Vivid auditory and visual hallucinations

Ictal features

- Cognitive disorders may follow status epilepticus
- Status epilepticus from focal dyscognitive seizures and absence seizures results in prolonged alterations of responsiveness
- Non convulsive status epilepticus can also present with immobility waxy flexibility and behavioural negativism resembling catatonia
- EEG's and a therapeutic trial of AED's is the only way to distinguish behavioural disturbances with non convulsive states

Automatisms

- Automatisms are conventionally associated with behaviour in ictal and post ictal delirium
- It is a more or less coordinated repetitive motor activity usually occurring when cognition is impaired and for which the subject is usually amnesic afterwards
- Brief automatisms can often be unnoticed and majority of them are brief however some can last upto 1 2 hours as well
- Patients always look somewhat dazed with vacant expressions

Oro alimentary	Lip smacking Lip pursing Chewing licking tooth grinding
Mimetic	Facial expressions suggesting emotional state such as fear
Gestural	Fumbling or exploratory movements with hand directed to self or environment
Hyperkinetic	Pelvic thrusting pedalling thrashing rocking movements
Dysphasic	Impairment of language without dysfunction of primary motor areas impaired comprehension anomia paraphasic errors
Gelastic	Bursts of laughter or giggling without appropriate affect
Vocal Verbal	Single or repetitive utterances consisting of sounds words

Peri ictal features

- Psychiatric disturbances can occur before seizures prodromal after seizures postictal or during intermittent seizure activity
- Prodromal symptoms begin at least 30 minutes before seizure onset last 10 minutes to 3 days and are continuous with irritability depression headache confusion
- Postictal period is characterized by a confusional state lasting minutes to hours or occasionally days Prolonged postictal confusion may particularly follow right temporal focal dyscognitive seizures

Peri ictal features

- Peri ictal psychotic symptoms often worsen with increasing seizure activity
- Psychotic symptoms alternate with seizure activity
- Alternating psychosis when patients are having seizures they are free of psychotic symptoms but when they are seizure free and their EEG has **forced** or **paradoxical normalization** they manifest psychotic symptoms

Peri ictal features

- An important peri ictal psychiatric disorder consists of brief psychotic episodes that follow clusters of generalized tonic clonic seizures ie Postictal psychosis
- The postictal psychosis of epilepsy emerges after a lucid interval of 2 to 72 hours the immediate postictal confusion resolves and the patient appears turn to normal The postictal psychotic episodes last 16 to 432 hours
- Often include grandiose or religious delusions elevated moods or sudden mood swings agitation paranoia and impulsive behaviours **but no perceptual delusions or voices are heard**

Post ictal delirium

- The clinical presentation is distinctive with a sudden onset of mixed psychotic and affective features most notably agitation following brief lucid interval after seizures
- While epileptic seizures characteristically begin abruptly recovery of normal function is usually gradual
- The patient slowly becomes aware of where he is and gradually interacts more appropriately
- Consciousness is more profoundly impaired following a generalised tonic clonic seizure and recovery more protracted
- Full recovery of consciousness may take much longer especially in the elderly or in patients with learning difficulties
- Most common in patients with TLE with bilateral lobe pathology

Inter ictal features

Interictal psychosis Schizophrenia like psychosis of epilepsy

- Most psychotic episode that occur in epilepsy are inter ictal
- They usually have no direct relationship to seizure events and their duration may vary from days to years
- Many of these patients develop worsening psychotic symptoms that are associated with an increase in seizure frequency or AED withdrawal
- Few patients also have worsening of psychotic symptoms on controlling of the seizures alternating psychosis
- Spontaneous resolution of interictal psychosis is not common but may occur in patients with late onset epilepsy or shorter duration of history

Characteristics of psychosis in TLE

- Paranoia with sudden onset
- Psychosis alternated with the seizures affect is preserved and personality is not deteriorated
- Less social withdrawal than schizophrenia and less systematized delusions
- More hallucinations than in schizophrenia
- Overally more positive as compared to negative symptoms

Predisposing factors for interictal psychosis

- Focal dyscognitive seizures with secondary generalized tonic clonic seizures
- History of epilepsy of 11 – 15 years
- Long interval of poorly controlled seizures
- Recently reduced seizure frequency
- Medio basal temporal lesions

Anatomically defined epilepsy syndromes

Seizures originating in different anatomical locations take characteristic forms

1. Temporal lobe epilepsy TLE MC 60
2. Frontal lobe epilepsy FLE 20 30
3. Occipital lobe epilepsy OLE 5 7
4. Parietal lobe epilepsy PLE 5

TLE

- Most varied and complex auras Epigastric aura fear Auditory olfactory gustatory hallucinations
- MCC is hippocampal sclerosis
- Cognitive abnormalities include disturbances of speech memory and thought
- D j vu and jamais vu is common
- Most frequent automatisms seen are lip smacking chewing swallowing fumbling grimacing wandering Post ictal nose rubbing is also common
- Dystonic posturing most commonly in arm is seen in 70 of patients

TLE

- Post traumatic aetiology is frequent however tumours and cortical dysplasia are more common
- Tend to begin and end abruptly ___ 1min
- Motor phenomenon Complex posturing and behavioural automatisms are most conspicuous feature
- TLE presentations are often bizarre and may be mistaken for dissociative convulsions frantic bilateral and often overtly sexual
- Vigorous clapping finger clicking grasping rubbing and pounding movements pelvic thrusting undressing and genital manipulation may be seen
- Patients often report partial awareness during these seizures and patients often do not report any ictal fear

OLE

- Frequently misdiagnosed as migraine in children and mimic other partial seizures in adults
- Elementary visual hallucinations are landmark but not seen in all and clinical features include headache confusion vomiting and visual disturbance
- Common causes of occipital lobe epilepsy include tumours trauma and developmental malformations
- Typically completely reversible with treatment of the underlying cause

PLE

- Very and most common aetiology is tumours
- Somatosensory auras are reported by some 80 of patients with elementary paraesthesia by far the most common feature tingling numbness prickling crawling or electrical sensations
- In a study done by Salanova et al 57 of patients showed unilateral clonic activity 28 showed tonic posturing and 17 showed oral automatisms

Personality disorders in epilepsy

- There is a high prevalence of personality disorders in patients with epilepsy including borderline atypical or mixed histrionic and dependent disorders
- Patients with personality disorders tend to show dependent and avoidant personality traits
- Epileptic patients frequently lack a stable character structure and can be immature and impulsive and this can explain the incidence of irritability and suicide attempts
- Psychosocial difficulties such as stigma fear and difficulty in getting jobs driving a car maintaining a marriage contribute to dependency and low self esteem

Personality disorders in epilepsy

- Although there is no general epileptic personality a group of traits termed the **Gastaut Geschwind syndrome** occurs in a subset of patients with focal dyscognitive seizures
- These patients give high significance to most things in life and are often serious humourless over inclusive and have an intense interest in philosophical moral and religious issues
- These patients during conversation tend to talk repetitively and circumstantially about a very restricted range of topics

Aggression

- Criminologist Cesare Lombroso promoted the association of epilepsy with aggressive sociopathic tendencies
- This association has been studied with stimulation of amygdala in cats which in turn showed aggressive verbalization
- Patients with left temporal lobe seizure foci showed higher scores on hostile feelings than other patients with epilepsy
- Antiepileptic medication like Levitiracetam may also trigger aggression and mood lability in some patients

Sexuality

- Patients with epilepsy tend to be hyposexual
- Men and women tend to experience disturbance in sexual arousal and a lower sexual drive
- Erotic fantasies and may experience even impotence or frigidity
- AED's can also cause undesirable effects such as ED retrograde ejaculation and altered semen quality

Mood disorders associated with epilepsy

- Depressive disorders MDD dysthymic disorder adjustment disorder
- Episodic mood disturbances with agitation and suicidal behaviour may occur with increasing seizure activity
- Manic features are rarely seen
- Anxiety disorders such as GAD panic disorder OCD phobias and social anxiety are the second most common psychiatric morbidity
- Some patients with epilepsy clearly have PTSD from psychological trauma of recurrent seizures

Psychogenic non epileptic seizures

PNES

- These are involuntary psychogenically induced spells that may mimic many epileptic behaviours

  Dissociative convulsions

- The previously used term 'Pseudo seizure' is discouraged
- They maybe differentiated from epileptic seizures using a video EEG recording however the diagnosis does not rule out epileptic seizures as nearly 10-15 of patients with PNES have a true seizure disorder

Epileptic Seizure	Non epileptic seizure
Preceded by aura	Generally not preceded by aura anxiety symptoms like breathlessness palpitation might be present
Stereotypical seizure pattern	Seizure may differ from attack to attack
Onset is abrupt with short duration 2 mins	Gradual onset with longer duration
Symmetrical clonic activity in GTC seizure	Asymmetrical movements pelvic thrusts hyperarching
Tonic rigidity at onset of GTC seizure	Whole body rigidity rare
Disturbed autonomic reactivity corneal reflex and pupillary reflex	Normal autonomic reaction and corneal and pupillary reflexes
Abnormal ictal EEG	Normal ictal EEG
Postictal delirium pseudosleep may be present prolactin increases 1000 UL 10 to 20mins postictally	No postictal delirium or pseudo sleep is present and no increase in prolactin

Malingered Seizure	Nonmalingered Nonepilieptic seizure
More common in men	Marked female predominance
Less likely to obtain prior abuse history and psychiatric history is generally not present	Prior history of physical or sexual abuse and prior psychiatric history is generally found
Evident secondary gain	No clear secondary gain
Seizures are completely under persons control and awareness of seizure is conscious	Involuntary and awareness of seizure is subconscious
Pt is often angry or anxious on confrontation and there is a lack of evidence for epileptic seizures	Indifferent detached feeling in patients

Neurodiagnostic tests

- Seizure and epilepsy are clinical diagnoses and several tests are used to identify provocative factors diagnose seizure syndromes
- In addition to routine labrotory test and toxicology screenings scalp EEG is the most widely used confirmatory test for diagnosing seizure disorders
- Video EEG done for extended amounts of time can be helpful in diagnosing seizures of unknown etiology
- Inpatient monitoring is very useful in distinguishing epilepsy from PNES
- Neuroimaging with CT MRI scans is useful in precisely visualising a seizure focus
- SPECT PET scans are used in patients who are candidates for epilepsy surgery

Management

- After a diagnosis of epilepsy is confirmed the first line of management is starting the patient on an appropriate AED

Generalised-Onset Tonic-Clonic	Focal	Typical Absence	Atypical Absence, Myoclonic, Atonic
First line Lamotrigine Valproic acid	Lamotrigine Carbamazepine Oxcarbazepine Phenytoin	Valproic acid Ethosuximide Lamotrigine	Valproic acid Lamotrigine
Alternative Phenytoin Carbamazepine Oxcarbamazepine Phenobarbital Primidone	Valproic acid Gabapentin Phenobarbital Primidone	Lamotrigine Clonazepam	Clonazepam Clobazam

Treatment in psychiatrically disturbed patients with epilepsy

- A first consideration behavioural effects of antiepileptic medications
- Carbamazepine and valproate significant antimanic and modest antidepressant properties They have an efficacy in the long term prophylaxis of manic episodes
- Lamotrigine is the only antiepileptic that has a well established efficacy in preventing recurrence of depressive episode in bipolar disorder
- Clonazepam in addition to its anxiolytic properties can serve as a supplement to other antimanic therapies

- Gabapentin and Pregabalin also decrease anxiety and improve general well being in some epilepsy patients
- Carbamazepine and Ethosuximide may have value for borderline personality disorder in reducing mood swing and behavioural disinhibition
- For interictal psychosis there is no difference in efficacy between FGCi's and SGCi's and therefore drugs should be chosen in view of their seizure threshold lowering effect
- Evidences from case reports suggest that haloperidol risperidone paliperidone and aripiprazole may be the least seizure threshold lowering agents in contrast to clozapine olanzapine quetiapine

- Antidepressants can alleviate both anxiety and mood symptoms at the same time and drug should be chosen based on tolerability and seizure threshold reducing effect
- Overdose and intoxication of tricyclic TCA and tetracyclic antidepressants TeCA and SNRIs have been well documented as one of the potential causes of seizure
- SSRIs Escitalopram and Sertraline can be used as first line anti depressants considering their tolerability
- Pregablin recently showed an antianxiety effect in small open labeled trial in patients with epilepsy and GAD Therefore it can be an alternative choice if the patient did not respond to the first SSRI

Drug interactions

- Antiepileptic drugs often increase the metabolism of a psychotropic drug which results in a decrease in therapeutic efficacy
- Withdrawal of AED's can precipitate rebound elevations in psychotropic levels
- Psychotropic drugs may cause competitive inhibition of AED's
- Older drugs such as phenytoin carbamazepine oxcarbazepine have high interactions with psychotropic medication and newer drugs such as Lacosamide Levitiracetam Clobazam Ethosuximide are relatively free of enzyme inhibiting or inducing properties
- Lamotrigine Increase Olanzapine and Aripiprazole Decrease Quetiapine
- Topiramate Increase Haloperidol Decrease Risperidone

Vagal Nerve Stimulation

- Vagal nerve stimulation was introduced as a treatment for epilepsy over 10 years ago Schachter 2002
- The procedure involves intermittent electrical stimulation of the vagus nerve via a stimulator inserted surgically over the anterior chest wall and the mechanism of action is unknown
- VNS is usually considered for patients who prove unsuitable for epilepsy surgery but there is some evidence of efficacy in generalised epilepsy
- Well tolerated but low seizure remission rate 5 10 and S E include hoarseness of voice and throat irritation during the procedure

Surgery in Epilepsy Management

- Up to a third of epilepsy patients may have seizures that are not fully controlled with medications
- For these patients resection of epileptogenic brain may offer a far better chance of seizure control than medication alone and the most commonly performed operation is temporal lobectomy improvement in frequency 80 and 60 are seizure free
- Patients with medial TLE are most commonly the ones receiving surgery
- Most commonly done surgery is anteromedial temporal lobectomy or disconnection of pathways of seizure propagation
- More selective amygdalohippocampectomy is also done

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THANK YOU