SEIZURES, EPILEPSY AND NEUROPSYCHIATRY

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Overview

• ILAE definitions (2012)
  – Seizure types – Epilepsy – Epilepsy Syndromes

• DD of seizures and some clinical ‘flags’

• Major neuropsychiatric syndromes
  – ‘Latency Period’ (post-ictal)
  – ‘Alternative Mental States of Epilepsy’ (Trimble, Schmitz 1998 - if EEG – ‘Forced / Paradoxical Normalisation’)
Epileptic seizure

‘A transient episode of neurological dysfunction caused by abnormal excessive or synchronous cortical neuronal electrical activity’ (ILAE, 2011)

• Variable clinical manifestations
  ➢ Location of the abnormal neuronal discharge
  ➢ Propagation patterns ~ on neuronal networks
    ➢ Unilateral - bi - or transhemispheric (C. callosum, fornices)

• To date, 2012 nomenclature slowly being adopted
  ➢ Focal (partial)
  ➢ Generalised
Epileptic Focus & Epileptic Zone

Presurgical evaluation:-

- HO ictal & interictal semiology
- 1.5T+ Neuroimaging
  - (structural / functional);
  - FLAIR - Identification of EZ
- EEG, VEEG, Neurophysiological
  - provocation
    - sleep / - deprivation, light (~30Hz), ‘reflex’ sz
- Other specialised neurophysiology
  - EPs; cerebral functional imaging, MEG, magnetic stimulation
  - Identification of functional deficit zone and lateralisation of eloquent cortex
    - fMRI [replaced Wada Test – intracarotid sodium amytal test]; interictal SPECT / PET sequence
    - Invasive intracranial (grid) recording
Epilepsy

‘A heterogeneous condition indicative of diverse underlying pathologies characterised by an increased susceptibility to spontaneous epileptic seizures’ (ILAE, 2012)

- 0.5-2% prevalence in population (1:10 on average)
- More common in childhood (up to 4%); > 55’s
- Incidence ~ 50-75/100,000 per year

- Epilepsy is epiphenomenon of differing brain diseases
  - adjusted ILAE diagnostic proposals (A. Berg et al., 2010 – 2012)
  - Implications for diagnosis of epilepsy & neuropsychiatric syndromes
Epilepsy – new aetiological classification

Old Terminology (ILAE, 2009+)

- Idiopathic
- Cryptogenic
- Symptomatic
- Focal (epileptic focus somewhere in network of ONE hemisphere)
- Generalised (epileptic focus .... In network rapidly engaging bilaterally distributed network)


- Genetic
- Structural / Metabolic
- Immune (incl. some epileptic encephalopathies > 40)
- Infectious

[most Epilepsy Syndromes incl. both seizure types]
Partial (focal) seizure

- Alertness – awareness - consciousness
- Simple (aura - awareness)
- ‘Complex’ (impaired consciousness)
- ‘Secondarily’ generalised
Clinical Semiology of Focal Seizures

- Frontal
  - Primary motor cortex
  - Supplementary motor area (SMA)
  - Other
- Temporal
  - Lateral/Neocortical
  - Mesial (hippocampal region)
- Parietal
  - Primary sensory cortex
- Occipital
Seizures arising from mesial temporal lobe

- Olfactory, gustatory hallucinations
- Fear, déjà vu, jamais vu, derealisation etc
- *Rising* epigastric sensation
- Psycho-motor arrest
- Altered awareness/consciousness
- Blank staring expression (graduated on – offset)
- Oro-lingual (lip-smacking, swallowing, chewing) manual automatisms
- Gestural automatisms
- Contralateral dystonic arm posturing
- Duration – minutes
- Post-ictal confusion, gradual recovery
How to *clinically* determine likely ‘epileptogenic focus / region’

**Lateralising signs in intractable partial epilepsy**

1. Sz semiology pre-, postically; x3 observers blinded to
   1. History; EEG, surgical resection  
      [N=166 seizures in N=38 patients];  
      [at least 2 raters concur]
   2. Epileptogenic region (ER) identified in 78%  
      (kappa .68; PPValue 94% 90%CI 87-100)

2. Sz semiology [extra-temporal cortex] – *contra* lateral ER  
   [more frequently extra-temporal] clinical indicators
   1. 45% had Head version – forced and sustained head deviation  
      (kappa .76; PPV 94%)
   2. 37% had dystonic posturing of upper extremities  
      (kappa .47; PPV 93%)
   3. 34% had unilateral mouth deviation  
      (kappa .83; PPV 92%)

3. Sz semiology [temporal cortex] – *ipsilateral* ER  
   clinical indicators
   1. Unilateral upper extremity automatism  
      (kappa .65; PPV 100%)
   2. Dominant hemisphere TL - postictal dysnomia  
      (kappa .89; PPV 100%)
   3. Non-dominant hemisphere TL - ictal speech  
      (kappa .75; PPV 83%)

**Summary:** TLE ER - higher probability if - dystonic posturing; postictal dysnomia, ictal speech, unilateral upper extremity automatism
How to clinically determine likely ‘epileptogenic focus’

2nd GTCS - Significance of gaze & head deviation

1. VEEG – clearly lateralised Sz focus (N = 92 sGTCS in N=29 patients)
2. blinded single rater - direction and type (forced v non-forced) head / gaze deviation
   1. Forced HD - sustained, unnatural, tonic or clonic movements
   2. Non-forced HD - sustained deviation similar to volitional head movements which are neither tonic nor clonic
3. 83 / 92 SGTCs (in 26 / 29 patients) had lateralised and sustained forced HD
   1. contralateral in 90% (72/83) of VEEG seizure onset, if
      1. Either progressed to a SGTC, or
      2. Commenced in 10 sec prior to seizure focus on VEEG
   2. ipsilateral in >90% (75/83) of VEEG seizure onset, if
      1. HD ended before the Sz began to generalise in VEEG (in all the HD ended 11+ sec before the SGTCS commenced)
   3. No lateralising significance if HD within first 10 sec after VEEG SGTCS onset

Summary:

Non-forced HD is of no lateralising significance
89% of Forced HD was contralateral to VEEG SGTC seizure onset

NY Langone Epilepsy Centre Group - Orine Devinsky, K. Perrine et al., Neurology, 1993, 43(7); 1308
The International 10 - 20 System of Electrode Placement

- Each electrode site has a letter to identify the lobe, along with a number or another letter to identify the hemispheric location.
  - F – Frontal lobe
  - T – Temporal lobe
  - C – Central lobe
  - P – Parietal lobe
  - O – Occipital lobe
  - “Z” refers to an electrode placed on the mid-line (‘Zentral’)
- Even numbers (displayed in blue in the image) refer to the right hemisphere and
- Odd numbers (displayed in red in the image) refer to the left hemisphere
- Nasal (G) reference electrode
Temporal Lobe Seizure EEG (L sided onset ~ T3 - F7)
Generalised Seizures

- Absence (petit mal)
- Myoclonic
- Tonic
- Clonic
- Tonic clonic (grand mal)
- Atonic
Absence Seizure (petit mal)

- Sudden onset
- Behavioural arrest
- Unresponsive
- Staring
- Minor blinking
- Short duration (seconds)
- Quick recovery
- Characteristic EEG
Myoclonic Jerk (seizure)

- Brief jerk(s)
- Usually involving upper limbs
- May affect legs and trunk
- Consciousness usually retained
- May show diurnal variation
- May be precipitated by alcohol withdrawal and sleep deprivation, EEG features
- Reflex seizures
  - Special case of myoclonic (general or focal)
Reflex seizures

- ‘Objectively, consistently & reproducibly evoked by specific sensory (afferent) stimulus / patient activity’ (ILAE, 2012)

  - Sensory elementary, unstructured (light flashes, startle, a monotone) or elaborate, structured stimuli tactile or proprioceptive stimuli

  - Patient activity may be elementary, e.g. motor (a movement – chewing, swallowing); or elaborate, e.g. cognitive function (reading, calculations, chess), or both (reading aloud).
Tonic seizures

- Usually sudden onset
- Symmetrical muscle contraction
- Consciousness usually impaired
- May result in forceful sudden falls
- Common during sleep
- EEG features
Atonic seizures

- Sudden onset
- Loss of muscle tone
- No apparent preceding myoclonic or tonic event
- Consciousness usually impaired
- Lasts approximately 1-2 seconds
- Involves head, trunk, jaw or limb musculature
- May result in sudden falls (drop attacks)
Generalised Tonic Clonic Seizure

- +/- ‘warning’
- Loss of consciousness
- Tonic contraction of muscles (jaw, trunk and limbs)
- Cyanosis
- Clonic jerking
- ‘Frothing at mouth’
- Tongue biting [LATERAL!]
- Piloerection (cave: room temperature; exposure)
- Incontinence
- Investigatory symptoms: biochemical & other changes
- Post-ictal features
Is it a Seizure?

- Accurate history from patient
- Accurate description from an observer
- Consider alternative diagnoses (>96% of aetiologies)
  - Syncope
  - Non-epileptic attack disorder (NEAD) or ‘Psychogenic, non-epileptic seizures’ (PNES)
  - Transient ischemic attack (TIA)
  - Transient global amnesia (TGA)
  - Other
    - CVA
    - ABI / TBI
    - ICP changes
Vasovagal Syncope

• Provocative factors
• Warning symptoms
• Clinical features
  - Colour
  - Involuntary Movements
  - Duration
  - Recovery
Syncope vs Convulsive Seizure

Vasovagal Syncope
Prodromal symptoms
lightheadedness, nausea
palpitation, sweaty, warmth, pallor,
dark/blurred vision,
giddy sensation, hearing tingling/pins&needles
muscular pains
hyptonia
Fall - brief – positional
post syncopal confusion

Seizure
Variable warnings
(Prodrome v SPS v CPS)
Fall
Initial tonic phase
Cyanosis
Clonic jerking
Duration (minutes)
Tongue biting (Post-ictal confusion)
Tongue biting Syncope v Convulsive Sz

Study design

• N = 106 prospective, consecutive epilepsy monitoring for known SGTCS
  – oral laceration yes/no
  – Central tongue v lateral tongue

VERSUS

• N = 45 retrospective study patients with syncope
• Seizure population:
  – N = 63 seizures in N= 34 / 106 patients on VEEG
    • Tongue laceration - N = 8 of N= 34 patients with VEEG seizures had laceration
    • All were lateral tongue lacerations
  – N = 1 / 45 with syncope had tongue laceration
  – at the tip of the tongue [i.e. not lateral]

• Summary
  – Seizure diagnostic sensitivity of tongue biting is 1:4 (24% in this study)
  – Seizure diagnosis specificity of lateral tongue biting is 99% for the diagnosis of GTCS

Non-epileptic seizures

• May resemble epileptic seizures
• Heterogeneous aetiology
• Clinical features may include
  ➢ waxing and waning pattern of movements
  ➢ variable rate and direction of jerking
  ➢ horizontal head movements
  ➢ eye closure and resistance to passive eye opening
• No electrophysiological correlate
• Videotelemetry
• Psychological evaluation
Investigations

• EEG
  – Routine
  – Ambulatory EEG
  – Vide-telemetry

• Brain Imaging
  – MRI
  – Functional imaging

• Blood tests
  – Routine
  – Special tests [PRL]

• Other
  – Mobile phone recordings (pre-onset)
  – CSF
Epilepsy Syndromes

- Common clinical features
  - Age of onset
  - Seizure types
  - EEG characteristics

- Syndrome recognition useful
  - Aetiologies to consider
  - Treatment choices
  - Prognosis
Epilepsy syndromes

- **Neonatal/infantile**
  - Self-limited familial neonatal epilepsy
  - West syndrome

- **Childhood**
  - Lennox-Gastaut syndrome
  - Childhood absence epilepsy
  - AD nocturnal frontal lobe epilepsy

- **Adolescent/adult**
  - Juvenile absence epilepsy
  - Juvenile myoclonic epilepsy

- **Variable age**
  - Temporal lobe epilepsy related to hippocampal sclerosis
  - Progressive myoclonus epilepsies
Childhood absence epilepsy

- Onset in childhood usually 5-8 (3-10)
- Girls > Boys
- Frequent absence seizures (up to 100/day)
- Characteristic EEG
  - Generalised 3 HZ spike and wave discharges
  - Hyperventilation induced seizures
- Positive family history of epilepsy
- Usually remits at puberty
- Ethosuximide, sodium valproate
Juvenile myoclonic epilepsy (JME, Janz Syndrome, 1981)

- Prevalence 10% of adolescent and adult epilepsies
- Onset age depends on seizure type
  - Absences (30%) 5 to 16 years
  - Myoclonus (100%) 12-16 years
  - GTCS (90%)
- M=F
- Circadian rhythm
  - Seizures, especially jerks, occur within 1 hour of awakening

Epilepsy Neuropsychiatry, Moeller Centre, Nov. 2016
Juvenile myoclonic epilepsy  (JME, Janz Syndrome cont.)

- Precipitating factors
  - Sleep deprivation
  - Fatigue
  - Alcohol
  - Emotional stress, excitement

- EEG
  - Irregular 3-6 Hz spike/polyspike and slow wave discharges
  - Photoparoxysmal responses
Juvenile myoclonic epilepsy (JME, Janz Syndrome cont.)

Management
- Lifestyle advice
- Sodium valproate
- Levetiracetam
- Lamotrigine
- Clonazepam
- Avoid carbamazepine

Prognosis
- Does NOT remit
- Seizures generally well controlled with appropriate medication in up to 90% of patients
Temporal Lobe Epilepsy

- Focal epilepsy accounts for 60-70% of all epilepsies
- 50% of focal seizures arise from temporal lobe structures
Hippocampal Sclerosis

CA1

CA2

CA3

CA4

dentate gyrus
Syndrome of mesial temporal sclerosis

- History of complicated febrile convulsions in infancy
- Latent period 3-20 years
- Complex partial seizures
  - Visceral, experiential auras
  - Behavioural arrest
  - Impaired consciousness
  - Oral and manual automatisms
  - Contralateral dystonic posturing of arm
  - Post-ictal confusion

Jan 17
Epilepsy Neuropsychiatry, Moeller Centre, Nov. 2016
Syndrome of mesial temporal sclerosis

• Neurological examination
  ➢ Normal
• EEG
  ➢ Normal
  ➢ Interictal abnormal activity in anterior temporal regions
    • Spikes/sharp and slow waves
    • Temporal intermittent rhythmic delta activity
  ➢ Ictal lateralised rhythmic theta activity
• MR Imaging
  ➢ Hippocampal atrophy/sclerosis
Hippocampal Sclerosis
Hippocampal Sclerosis

hippocampal atrophy

T2 hyperintensity within hippocampus = gliosis
TLE due to mesial temporal sclerosis
Prognosis and Management

• Increasing refractoriness to antiepileptic medication
• Consequences of medically refractory epilepsy
• Potential candidates for
  ➢ Epilepsy surgery
  ➢ Vagal nerve stimulation Therapy (VNS)
    ➢ Incl. post – epilepsy surgery!!
Neuropsychiatry in Seizures & Epilepsy Syndromes

• Interictal
• Prodrome
• Peri-ictal
  – simple partial / aura
  – focal CPS
• Ictal
• Post-ictal
• ‘Alternative Mental States of Epilepsy / Paradoxical - / Forced Normalisation
Ictal Neuropsychiatry

- Ictal Anxiety (common, 1/3 of patients, R>L TLE)

- Ictal depression (rare; R FL > other network nodal points)

- Ictal psychotic (sensory, not well ‘defined’)

- Ictal aggression (Delgado-Escueta et al., 1988; 1992)
Peri-ictal

• Prodromal / pre-ictal
  – ‘differing’ behavioural phenotype from normal presentation, recognisable, definite change

• Post-ictal
  – Psychosis [LATENCY of up to 7/7]
  – Confusional state (re-active aggression)
  – Affective mood disturbances
    • Manic state
    • Depression
    • Anxiety
Interictal

- Depression (2:10 to 4:10 individuals)
  - Interictal Dysphoric Disorder (D. Blumer, 2000)

- Anxiety
  - GAD > Panic Disorders > Phobias > OCDs

- Bipolar disorder (< 5%; R > L hemisphere)

- NB: Interictal psychosis is either a
  - Schizophrenia (F20.0), or
  - Epilepsy ~ psychosis (F07.0) with different semiology & developmental trajectory)
‘Alternative Mental States of Epilepsy / ‘Paradoxical – ‘/ ‘Forced Normalisation’

• an electro-clinical phenomenon
• If no EEG available – ‘AMS of Epilepsy’
• If EEG available
  – ‘Paradoxical – ‘ (clinical emphasis), or
  – ‘Forced Normalisation’ (of the EEG)
• Risk: Chronic epilepsy, sudden improvement 2^{nd} to
  – Anticonvulsant
  – Epilepsy Neurosurgery
  – Never VNS!!!
• ILAE Classification worth looking at (A. Berg et al. 2010 onwards; Panyatopoulos, 2012)
  – superb interdisciplinary Behavioural Neurology
    • annual ILAE Chapter meeting
    • Biannual (alternating) European (28!!) / Asia / World Congress

• If nothing else, remember
  – LATENCY PERIOD of 7/7 – tx target is the sz!
  – ‘Alternative Mental States of Epilepsy’
    • Anticonvulsant ~
    • Neurosurgery
    • Never found in VNS!!!!

• Ring for advice – if uncertain!