Types of epilepsy syndromes and their value

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Elaine Hughes
Kings College and Evelina Children’s Hospitals
The concept of an epilepsy syndrome

• age related
• characteristic seizure(s) - may evolve over time
• may have typical EEG
• may provide clues to aetiology
• may have associated cognitive phenotype
• outcome may be known and treatment response predictable

‘a complex of clinical features, signs and symptoms that together define a distinctive, recognizable clinical disorder’.
ILAE classification 1970 – H Gastaut

seizure type
ictal and interictal EEG correlate
anatomical substrate
aetiology
age
ILAE Classification 1989

comment

‘...the limitation of the ICE (international classification of epileptic seizures) which is confined to description of individual seizure types ...

is that the terminology used in daily communication between colleagues consists of description of syndromes.’
ILAE proposed classification 2001

is it an epileptic seizure? axis1
if so, what type? axis2
is it part of an epilepsy syndrome? axis3
is there a defined aetiology? axis4
are there any additional impairments axis5

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Principles of current system

1. Mode of seizure onset
2. Syndromes and epilepsies
   (a) electroclinical syndromes
   (b) constellations
3. Aetiology
   (a) genetic
   (b) structural/metabolic
   (c) unknown cause
4. Other dimensions
Electro-clinical syndromes arranged by age of onset

Benign familial neonatal szs
Early myoclonic encephalopathy
Ohtahara syndrome

Migrating partial szs of infancy
West syndrome
Myoclonic epilepsy in infancy
Benign infantile seizures
Benign familial infantile seizures

Dravet’s syndrome (SMEI)
Myoclonic encephalopathy in non-progressive disorders

Febrile szs plus
Electro-clinical syndromes arranged by age of onset

- Epilepsy with myoclonic absences
- Early onset childhood occipital epilepsy (Panayiotopoulos)
- Epilepsy with myoclonic atonic (was astatic) seizures
- Lennox-Gastaut epilepsy
- Epileptic encephalopathy with continuous spike wave in sleep including Landau Kleffner syndrome (LKS)
- Childhood absence epilepsy
- Benign childhood epilepsy with centrotemporal spikes
- Late onset childhood occipital epilepsy (Gastaut)

- Autosomal dominant frontal lobe epilepsy
- Juvenile absence epilepsy
- Juvenile myoclonic epilepsy

etc.
The electro-clinical syndrome

To illustrate the use of this concept in clinical practice

1. Idiopathic / genetic (previously ‘benign’) focal epilepsies
2. Epileptic encephalopathies
‘benign’ epilepsy syndromes

Involves seizures which are self-limited in that spontaneous remission, regardless of treatment, occurs at an expected age and is the anticipated outcome in the vast majority of cases.

The consequences, if any, of the seizures are generally not disabling over the course of the active seizure disorder.

This does not preclude an increased risk of subtle to moderate cognitive and behavioral disorders prior to, during, or extending beyond the active phase of the seizures.

ILAE commission on classification and terminology July 2009
Electro-clinical syndromes arranged by age of onset

Febrile szs plus

Epilepsy with myoclonic absences
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Autosomal dominant frontal lobe epilepsy
Early onset childhood occipital epilepsy (Panayiotopoulos)

common

St Thomas series: prospective clinico-EEG study of consecutive children referred for EEG age 3-12 years: 7% (13/182)

benign

but encephalitis was common differential diagnosis at time of referral

Stormy onset with prolonged loss of consciousness in benign childhood epilepsy with occipital paroxysms

Cerebral insult-like partial status epilepticus in the early onset variant of benign childhood epilepsy with occipital paroxysms
Clinical features

- Behavioural change, headache often occur at onset
- Autonomic symptoms - nausea, retching, vomiting, pallor
- Pupillary changes, urinary and faecal incontinence – flaccid, unresponsive
- Confusion, eye deviation, speech arrest, hemi or generalised szs may develop

Common in age group 2 - 6 years - seizures mainly arise from sleep
Frequency typically low - single episode only in about 30%

Duration - minutes to hours - but no record of cognitive or neurological sequelae
benign childhood epilepsy with occipital paroxysms - Gastaut type

non visual symptoms

    focal seizures akin to TLE
    tonic clonic szs (13%) or hemiclonic sz

post ictal symptoms

    diffuse headache
    nausea and/or vomiting

A new type of epilepsy: benign partial epilepsy of childhood with occipital spike-waves

*NB symptomatic occipital seizures produce similar semiology*
# Syndromic Classification

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<td><em>More clarity about evolution of disorder</em> (i.e., prognosis)</td>
<td><em>False sense of security - desire for clarity</em></td>
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<td><em>Reduction in unnecessary investigations</em></td>
<td><em>May not uncover aetiology if ‘content’ with syndromic diagnosis</em></td>
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<td><em>Awareness of possible comorbidities</em></td>
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Current ILAE concept of epileptic encephalopathy

‘Can present along a continuum of severity and may occur at any age (but) … is most common and severe in infancy and early childhood where global and profound cognitive impairment may occur. Adults, however, can also suffer cognitive losses over time from uncontrolled seizures.

The epileptic activity itself may contribute to severe cognitive and behavioral impairments above and beyond what might be expected from the underlying pathology … and … these can worsen over time’.

Hope that rapid effective intervention should and can be used before the abnormal epileptic activity interferes irrevocably with normal processes of brain development.
epileptic encephalopathies

epileptiform abnormality on EEG

‘encephalopathy’
- altered cognition – global or specific
- altered interaction and awareness
- altered motor function
- altered behaviour

+/- manifest epileptic seizures
epileptic encephalopathy

points to note:

1. the EEG signature of an epileptic encephalopathy is often age specific rather than disease specific:
   - burst suppression → hypsarrhythmia → GSSW

2. the encephalopathy can:
   - arise de novo eg LKS, ‘idiopathic’ West syndrome
   - or on background abnormality eg TS, other developmental or acquired brain lesions

3. there is evidence for ‘impairment’ of function with a widening gap relative to peers
EEG signature of an epileptic encephalopathy often age specific rather than disease specific:
# Syndromic Classification

## Advantages

- *Improves treatment decisions:* avoidance of certain AEDs, choice of specific AEDs, consideration of other treatment modalities

- May guide research

## Disadvantages

- *Treatment by syndrome may distract from optimal treatment* e.g.
  - focal pathology driving West syndrome,
  - GLUT1 manifesting as myoclonic absences

- Current paradigm may become obsolete
Dravet

Is it actually an epileptic encephalopathy?
Is it the gene or the epilepsy that causes the difficulties?
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<th>Clue to Early Diagnosis</th>
<th>non DS (50)</th>
<th>DS (46)</th>
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<tr>
<td>Mean age at onset (months)</td>
<td>8.2</td>
<td>5.2</td>
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<tr>
<td>Onset &lt; 7 months</td>
<td>34%</td>
<td>93%</td>
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<tr>
<td>5 or more seizures before a year of age</td>
<td>16%</td>
<td>89%</td>
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<tr>
<td>Hemi-convulsions</td>
<td>2%</td>
<td>72%</td>
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<tr>
<td>Seizures longer than 10 mins</td>
<td>6%</td>
<td>80%</td>
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<td>Hot water induced seizures</td>
<td>6%</td>
<td>59%</td>
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Dravet – aetiology and outcome

aetiology
80% SCN1A mutations may be truncating or missense and poor genotype-phenotype correlation

development and prognosis
usually normal initially but often marked impairment with emergence of myoclonus and majority have significant learning difficulties
later problems with gait
high mortality from status and SUDEP
Dravet spectrum

Genetic Febrile Epilepsies and Associated Mutations

Dravet syndrome (Ds)
(Severe myoclonic epilepsy of infancy-SMEI)
SCN1A, SCN2A, SCN1B, and GABRG2, SCN9A as modifier

SIMFE
SCN1A

EMRF
PCDH19

GEFS+
SCN1A, SCN2A, SCN1B, GABRD, and GABRG2

FS/FS+
FEB1, FEB2, SCN1B, SCN1A, GABAA, GABRG2

SMEI-
Borderland
SCN1A

ICE-GTC
SCN1A
Aetiology is a vital component in classification.

**Genetic:** The epilepsy is a direct result of the known presumed genetic defect, e.g., Dravet’s (SCN1A etc), ADNFLE, ADPEAF.

**Structural/metabolic:** May include acquired lesions such as stroke, infection, antibody-mediated epilepsies, but also developmental brain malformations, including TS; and glucose transporter disorders where genetics also important.
syndromic classification

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<td>may guide research</td>
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order versus creativity?