

Outline

- Nocturnal Epilepsies
- Nocturnal Frontal Lobe Epilepsy (NFLE)
- Autosomal Dominant NFLE
- Distinction from Parasomnias

Sleep and Epilepsy

- Sleep-wake cycle has a profound effect on many epilepsies
- Vulnerable times for epilepsies
 - Sleep-wake transitions
 - Stage II
- Purely nocturnal epilepsies
 - Frontal Lobe Epilepsy
 - Temporal Lobe Epilepsy (less common)
 - Idiopathic Generalized Epilepsy (uncommon)

Activation of Epilepsies by Sleep

- Idiopathic Generalized Epilepsy
 - Uncommon (cf sleep deprivation)
- Symptomatic Generalized Epilepsies
 - Often
 - Tonic seizures may only appear in sleep
- Idiopathic Partial Epilepsies
 - Usual
 - Special case of Continuous Spike Wave in Slow Wave Sleep
- Symptomatic Partial Epilepsies
 - Usual
 - Sometimes Tonic -clonic seizures only in sleep

Nocturnal Frontal Lobe Epilepsy

Partial seizures are often brief and frequent

Seizures typically last about 30 sec (cf 2 min in TLE)

May have clusters of many per night

Auras simulating TLE may occur

Status epilepticus frequent in some series

Complex partial, tonic-clonic

EEG localization often difficult

Nocturnal Frontal Lobe Epilepsy

Frontal lobes are large; manifestations vary

Dorso-lateral surface; easily recognized
Lateralized eye/motor manifestations

Orbital and mesial surfaces; can have unusual features
Hypermobility complex partial seizures
Motor, vocal & sexual automatisms

Aetiology

Symptomatic - Tumour, trauma, infarct etc
Genetic
Unknown

Autosomal Dominant Nocturnal Frontal Lobe Epilepsy

Scheffer et al 1994, 1995

- Age of onset 2m - 52y (mean 12yr; median 8yr)
- Clusters of nocturnal seizures (median 6 per night)
 - Aura on awakening (70%)
 - Tonic spasms
 - Hyperkinetic motor seizures
 - Rare tonic-clonic seizures
- Normal examination and intellect (usually)
- Interictal EEG abnormalities very rare
- Misdiagnosed as normal sleep, parasomnias, hysteria etc
- Usually responds to carbamazepine

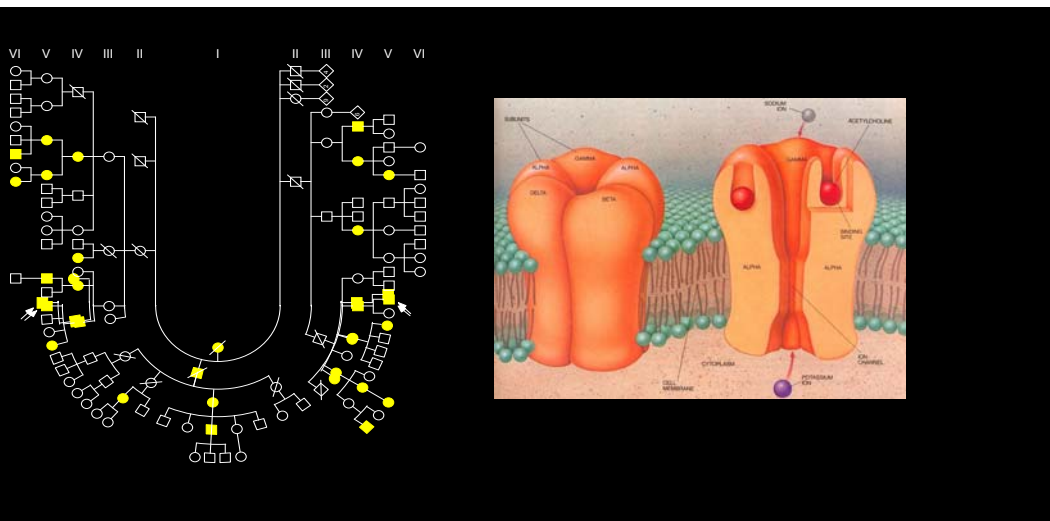
Autosomal Dominant Nocturnal Frontal Lobe Epilepsy

Clinical Genetics ADNFLE

- Autosomal dominant; penetrance 75%
- Marked intra-familial variation in severity
- Inheritance easily overlooked as relatives may be mildly affected

Other Familial Forms

- Some families show complex inheritance
- ? Relationship to parasomnias



The image contains two diagrams. On the left is a pedigree chart showing inheritance across six generations (I-VI). Affected individuals are marked with yellow symbols. On the right is a diagram of a nicotinic acetylcholine receptor channel. It shows a subunit with alpha, beta, gamma, and delta domains. The channel is embedded in a cell membrane, with the cytoplasmic side containing a beta-gamma complex and a gamma-Delta complex. The extracellular side has a binding site for acetylcholine. Labels include: SUBUNIT, ALPHA, BETA, GAMMA, DELTA, CYTOSOL, CELL MEMBRANE, ACETYLCHOLINE, and ION CHANNEL.

**Mapped to 20q
Nicotinic receptor**

**First epilepsy gene (1995)
Epilepsy Channelopathies**

Frontal Lobe Epilepsy and Parasomnia (FLEP) Scale

Discriminatory components on history

NFLE

Duration < 2min
Events in first 30 mins
Multiple events per night
Complex behaviour uncommon
Highly stereotyped
Often full recall of event and speech

Parasomnia

Duration >10min
Events later in the night
One or two events per night only
Often wandering and complex behaviour
Variable semiology
Event and speech during event not recalled

Validation

- Known parasomnia or NFLE, established to level of current gold standard
- Detailed descriptions of events by telephone interview; patient and witness
- Blinded application of FLEP scale by 2 independent interviewers
- Statistical analysis

FLEP Scale - Questions

Duration

| | | |
|--|----------|----|
| What is the duration of a typical event? | < 2 min | 1 |
| | 2-10 min | 0 |
| | >10 min | -2 |

Clustering

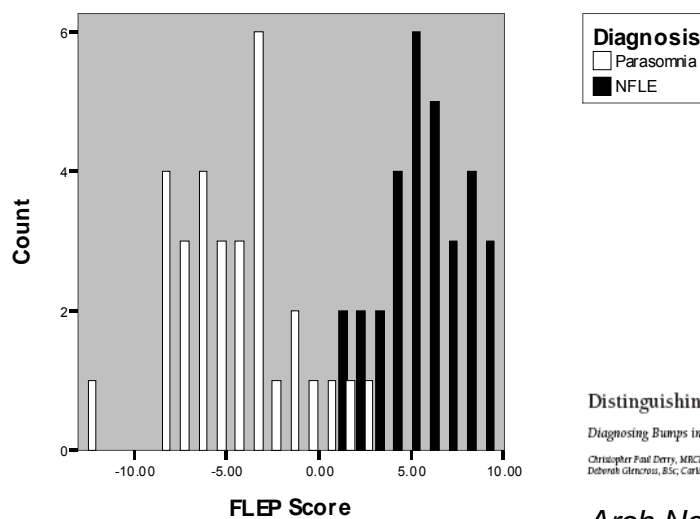
| | | |
|--|--------|---|
| What is the typical number of events to occur in a single night? | 1 or 2 | 0 |
| | 3-5 | 1 |
| | >5 | 2 |

Timing

| | | |
|--|--|---|
| At what time of night do the events most commonly occur? | | |
| | Within 30 min of sleep onset | 1 |
| | Other times (including if no clear pattern identified) | 0 |

Etc..

FLEP Score: Parasomnias vs NFLE



Distinguishing Sleep Disorders From Seizures

Diagnosing Bumps in the Night

Christopher Paul Derry, MRCP; Margee Davy, FRACP; Murray Johns, FRACP; Katie Kron, BSc; Deborah Glencross, BSc; Carlos Marin, PhD; Ingrid E. Schaffer, PhD; Samuel F. Berkovic, MD

Arch Neurol 2006; 63: 705

Key Features on History

- Likely NFLE
 - Short duration (< 2 minutes)
 - Multiple events (> 5 per night)
 - Lucid recall
 - Highly stereotyped
- Likely Parasomnia
 - Long events (> 10 min)
 - Wandering around home
 - Variable semiology

Conclusions

- Some epilepsies are exclusively nocturnal
- NFLE creates major problems in differential diagnosis
- Familial and sporadic forms
- Some families have nicotinic receptor mutations
- Clinical scale is useful in distinguishing NFLE from parasomnias