Clinical update on Sleep-related Hypermotor Epilepsy

SLEEP AND EPILEPSY ARE COMMON BEDFELLOWS
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Steve Gibbs, MD
Center of Advanced Research in Sleep Medicine
Hôpital du Sacré-Cœur de Montréal, Université de Montréal
Presenter disclosure

- Steve Gibbs, Neurologist at CARSM, Université de Montréal

- Potential for conflicts of interest:
  - No conflicts of interest in regards to this presentation
Objectives

1) What is SHE (Sleep-related Hypermotor Epilepsy)?

2) Review the historical background of SHE

3) Review patients characteristics and seizure semiology in SHE

4) Highlight clinical features that have a localizing value in SHE
Definition of SHE

What is SHE (Sleep-related Hypermotor Epilepsy)?
Consensus conference – Two major outcomes

- The need to change nomenclature
- The need to recognize the disorder as a distinct epilepsy syndrome
NFLE -------> SHE

• **Sleep-related**
  ✓ Sleep, rather than time of day, is critical
  ✓ Seizures may originate outside the frontal lobe

• **Stereotyped, abrupt, hypermotor seizures**
  ✓ “Hypermotor” includes seizures with vigorous hyperkinetic features and seizures with asymmetric tonic or dystonic posturing
Historical background

From «NPD» to «NFL» to «SHE»
Described 6 patients (17-32y) with repetitive abnormal and violent behavior during sleep, unresponsive to environment, for which they were completely amnesic.

Negative family history for epilepsy or NREM parasomnias
Episodic Nocturnal Wanderings Responsive to Anticonvulsant Drug Therapy

Timothy A. Pedley, MD, and Christian Guillemainault, MD

- All patients had normal wake-sleep cycles
- 3/6 had right anterior temporal epileptiform discharges
- All patients responded to CBZ or PHT.
- Although conclusive proof was lacking, hypothesized to be unusual complex partial seizures (resembled orbitofrontal seizures)
Nocturnal paroxysmal dystonia

E LUGARESI, F CIRIGNOTTA, P MONTAGNA

From the Institute of Neurology, University of Bologna, Italy

- Short lasting attacks of dystonic movements and/or ballic and/or choreoathetoid movements during NREM sleep (different from Pedley and Guilleminault)

- Absence of epileptiform abnormalities

- Responded favorably to low dose CBZ
Nocturnal Frontal Lobe Epilepsy


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Nocturnal Frontal Lobe Epilepsy

Montagna et al. 1990; Tinuper et al. Epilepsia 1999; Nobili et al. 2003
Epidemiology of SHE

• Pure-sleep epilepsies (>90%) represents around 12%

• SHE in the adult population: estimated minimum prevalence of 1.8-1.9/100 000

• Epilepsy surgery clinic (Niguarda Hospital database): 9.4%
  o 24% of drug-resistant frontal or frontal-plus cases
  o 4% of drug-resistant extra-frontal cases

• Undiagnosed? Many cases of SHE are misdiagnosed as parasomnias, especially in children

Thomas et al. 2010; Derry et al. 2013; Vignatelli et al. 2015; Gibbs et al. in prep
Differential Dx of SHE

Major episodes: challenging cases

Stereotypic behavior

Heterogeneous behavior

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Seizures in SHE

- Seizure begin before the age of 20 y (childhood-adolescence)
- Clinical features common to the genetic and localization-related forms
- Seizures types:
  - Major attacks (NPD)
  - Paroxysmal arousals
  - Minor motor events
  - Epileptic nocturnal wanderings

Seizures in SHE

- **Major attacks**: stereotyped movements of 20-30 seconds’ duration characterized by asymmetric tonic or dystonic posturing, ballistic or other complex movements

Tinuper et al. Neurology 2016; Gibbs et al. Sleep Med Rev 2016; Gibbs et al. in prep
Seizures in SHE

- **Paroxysmal arousals**: frequent 5-10s arousals with abrupt stereotyped movements of the trunk with head elevation +/- vocalization

- «Fragments» of major seizures

- Not diagnostic

Figure 3.—Video images (upper part) and stereoelectroencephalography (lower part) of a minor event (A), a precocious arousal (B), and a yawn (C). The progressive complexity of the motor behaviors and the different duration, amplitude, and spread of the epileptic spike are depicted. Dotted and continuous vertical arrows correspond respectively to the upper and lower photographs. Letters indicate the anode electrode. Bipolar derivations of 2 contiguous leads were employed. The traces show the electrical activity recorded from the following sites:

| F 2-3 | Right supplementary motor area (SSMA) |
| F 3-4 | Right V5A |
| M 1-2 | Right SSMA |
| M 1-4 | Right SMA |
| L 2-3 | Right ventral insular gyrus (CG) |
| H 1-2 | Right anterior CG |
| G 1-2 | Right premotor CG |
| N 1-2 | Right primary somatosensory cortex |
| M 11-12 | Right middle frontal gyrus |

| L 1-15 | Right precentral gyrus |
| F 6-9 | Right middle frontal |
| H 11-12 | Right inferior frontal |
| G 7-8 | Right inferior frontal |
| V 11-12 | Right middle frontal |
| X 12-13 | Right inferior frontal |
| A 1-2 | Right angular gyms |
| A 12-13 | Right middle temporal |
| M 1-2 | Left SMA |
Seizures in SHE

- **Minor motor events**: short-lasting (2-4 s) stereotyped movements interesting the limbs, the axial musculature and/or the head (recurring periodically)

- Non-specific (micro-) arousals

Seizures in SHE

Minor motor events and arousal instability

**SHE: seizure semiology**

Review of 135 patients with drug-resistant SHE  (*115 Engel I*)

<table>
<thead>
<tr>
<th>Characteristics of drug-resistant SHE</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of seizure onset</td>
<td>5.8 ± 4.4 years</td>
</tr>
<tr>
<td>Duration of disease</td>
<td>19.9 ± 10.3 years</td>
</tr>
<tr>
<td>Seizure frequency</td>
<td>64% daily; 90% weekly</td>
</tr>
<tr>
<td>EEG Abnormality</td>
<td>Abnormal in 82%; Localizing 48%</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>65%; 52% with « probable focal cortical dysplasia »</td>
</tr>
</tbody>
</table>

Gibbs et al. Submitted
SHE: seizure semiology

classification of early frontal
seizure semiology according to
the a four cluster-type
classification

temporal regions that form the early
read network in frontal lobe
seizures

SHE: seizure semiology

Classification of early frontal seizure semiology according to a four cluster-type classification

Cortical regions that form the early read network in frontal lobe seizures

SHE: seizure patterns (SP)

P 1: early elementary motor signs: early clonic signs, asymmetric tonic/dystonic postures and/or asymmetric facial contraction

2: non-integrated hypermotor movements

3: integrated hypermotor movements

4: gestural behaviors with high emotional content
SHE: seizure patterns (SP)

1: early elementary motor signs

2: non-integrated hypermotor movements: unanatural or anarchic gestural hypermotor movements with axial tonic postures and/or symmetric facial contractions

3: integrated hypermotor movements

4: gestural behaviors with high emotional content
SHE: seizure patterns (SP)

1: early elementary motor signs
2: non-integrated hypermotor movements

3: **integrated hypermotor movements**: hyperkinetic behaviors (pedaling, kicking, pelvic thrusting, etc), distal stereotypies and/or manipulation behaviors

4: gestural behaviors with high emotional content
SHE: seizure patterns (SP)

1: early elementary motor signs
2: non-integrated hypermotor movements
3: integrated hypermotor movements

4: gestural behaviors with high emotional content: integrated gestural behavior fear, fight or flight behavior, frightened facial expression and/or automatic signs.
SHE: seizure patterns (SP)

P 1: early elementary motor signs

P 2: non-integrated hypermotor movements

P 3: integrated hypermotor movements

P 4: gestural behaviors with high emotional content
HE: frontal SOZ (74 patients)

Antero-posterior organization of seizure semiology in SHE

Encircled spheres represent SOZ defined by stereo-EEG

Gibbs et al. Submitted
SHE: extra-frontal SOZ (41 patients)

6% of patients with SHE
- Temporal SHE (n=14)
- Operculo-Insular SHE (n=18)
- Posterior SHE (n=9)
SHE: extra-frontal SOZ (41 patients)

Temporal SHE tend to produce integrated behaviors with high emotional content (SP 3-4).

Perculo-Insular and posterior SHE share more elementary behaviors (SP 1-3).

Gibbs et al. Submitted
Is it possible to localize SOZ in SHE based on seizure semiology?
Locaizing value of nonmotor semiology

Nonmotor semiology in SHE is common in SHE (70%)

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Frontal</th>
<th>Temporal</th>
<th>Op-insular</th>
<th>Posterior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>49/74 (66%)</td>
<td>8/14 (57%)</td>
<td>15/18 (83%)</td>
<td>8/9 (89%)</td>
</tr>
<tr>
<td>Type of nonmotor manifestations (n)</td>
<td>Sensory (10)</td>
<td>Epigastric (3)</td>
<td>Sensory (11)</td>
<td>Sensory (5)</td>
</tr>
<tr>
<td></td>
<td>Emotional (12)</td>
<td>Emotional (2)</td>
<td>Epigastric (2)</td>
<td>Visual (2)</td>
</tr>
<tr>
<td></td>
<td>Cephalic (8)</td>
<td>Autonomic (2)</td>
<td>Auditory (1)</td>
<td>Auditory (1)</td>
</tr>
<tr>
<td></td>
<td>Epigastric (8)</td>
<td>Illusory (3)</td>
<td>Undefinable (1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Autonomic (6)</td>
<td>Cognitive (2)</td>
<td></td>
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Gibbs et al. Submitted
Localizing value of nonmotor semiology

Post-ictal confusion: retrospective data available in 101 patients (88%)

Present in 25% of cases

Significantly more frequent in temporal SHE
- Frontal (19%)
- **Temporal (67%)**
- Operculo-insular (13%)
- Posterior (28%)
localizing value of ictal features (EEG)

Patient selection: SHE with stereo-EEG recording + Engel I outcome

- Analysis of 107 frontal seizures and 40 extra-frontal seizures

Electrographic seizure duration was significantly shorter in frontal SHE
(39 ±40 sec vs. 62 ±25 sec)

Clinical seizure duration was also significantly shorter in frontal SHE
(32 ±35 sec [range 5-174] vs. 52 ±21 sec [range 20-117])

Gibbs et al. Epilepsia 2018
Clinical seizure lasting more than 40 sec yielded a sensitivity of 55% and a specificity of 90% for an extrafrontal onset.
Localizing value of ictal features (EEG)

Latency between the first video-detectable movement (often wakening) and the start of the hypermotor seizure was significantly shorter in frontal SHE (2 ± 2 sec vs. 11 7 sec)

Latency of less than 5 sec yielded sensitivity of 75% and a specificity of 90%
Conclusion

SHE (NFLE) is an epileptic disorder of heterogeneous etiology than is now increasingly recognized and better defined. It is an uncommon disorder but relatively frequent in specialized epilepsy and sleep clinic with frequent misdiagnosis. Seizure semiology is complex and varied but specific clinical and electrophysiological features can be considered to increase diagnostic accuracy.
Acknowledgments

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XYZ