Sleep disturbance in childhood epilepsy: clinical significance, assessment and treatment

Professor Gregory Stores
MD MA DPM FRCPsych FRCP
University of Oxford
Historical aspects

Aristotle (4th cent BC)
“Sleep is similar to epilepsy and in some way sleep is epilepsy”

Soranus (2nd cent)
Untreated nightmares lead to epilepsy

Both epilepsy and sleepwalking affected by the moon (John of Gaddesden 14th cent)

Thomas Phaire (1545)
Childhood sleep problems and epilepsy
Watchyng out of measure

Terryble dreames and feare in the sleepe

Colyke and rumblyng in the guttes

Pyssyng in bedde
“Of Watchyng Out Of Measure”

“Slepe is the nouryshment & foode of a sucking child, and asmuch requisite as yᵉ very teate, wherfore whā it is depreiued of the naturall rest, all the hole body falleth in distēper: cruditie and weakenes … vapours and fumes aryse into the head, and infect the braine, by reason whereof the child can not slepe, but turneth& vexeth it self wᵗ crying. Therefore it shalbe good to prouoke it to a natural slepe thus…”

Thomas Phaire 1545
Effects of children’s sleep disturbance

Child
- Emotional state and behaviour
- Cognitive function
- Educational progress
- Physical health (growth, immunity etc)

Parents
- Stress including sleep loss, anxiety, depression
The fallyng euyll called in the greke tonge epilepsia

“…lytle chyldren, are oftentimes afflicted, with this greuouse syckenes… sometyme by euyll and vnholosome diet, whereby there is engendred many colde and moyst humours in the brayne, whereupon this infirmity procedeth.”

“Saphires, smaragdes, red coral, piony, mystletow of the oke… and the stone that is founde in the bellye of a yong swallow…These or one of them, hanged about the necke of ye chyld, saueth and preserueth it from the sayd sickenes.”

Thomas Phaire 1545
Aspects

Effects of sleep factors on epilepsy and *vice versa*

Types of sleep disturbance in children with epilepsy

Aetiology of sleep disturbance in children with epilepsy

Diagnostic confusions
- Sleep disorders confused with epilepsy
- Epilepsies confused with sleep disorders
- Epilepsy and OSA

Basic principles of assessment and treatment
Details

Stores G. Sleep disturbance in childhood epilepsy: clinical implications, assessment and treatments. Archives of Disease in Childhood ADC Online, first published April 26th 2013 as 10.1136/archdischchild-2013-303825
Generalisations are few

Diversity of epilepsies

Aetiology
Clinical manifestations
Natural history
Severity
Responsiveness to treatment
Physical and psychiatric comorbidities

80+ sleep disorders officially recognised
Sleep problems v sleep disorders

Three sleep problems
- Insomnia
- Excessive sleepiness
- Parasomnias (unusual behaviours, experiences, movements associated with sleep)

80+ sleep disorders (ie possible underlying causes of these problems)
The International Classification of Sleep Disorders

Second Edition
Diagnostic & Coding Manual

American Academy of Sleep Medicine
ICSD-2 categories with examples

Insomnias (psychological and physical causes)
Sleep related breathing disorders (OSA)
Hypersomnias of central origin (narcolepsy)
Circadian rhythm sleep disorders (shift work disorder, DSPS)
Parasomnias (sleepwalking)
Sleep related movement disorders (restless legs syndrome)
Isolated symptoms and normal variants (sleep talking)
Other sleep disorders (environmental sleep disorder)
Effects of sleep factors on epilepsy
A. Effect of the circadian sleep-wake cycle

‘Nocturnal grand mal’ (Gowers 1885)

‘Awaking grand mal epilepsy’ (Janz 1962)

Juvenile myoclonic epilepsy on waking or falling asleep
Architecture of overnight sleep (hypnogram)
B. Effect of sleep stage

Gowers (1985) two peaks of nocturnal seizures
(2 hours after sleep onset, 3-5am)

Partial seizures mainly stage 2 NREM
C. Activation of interictal epileptogenic discharges by sleep and sleep deprivation

**Sleep**
- Benign Rolandic epilepsy (BRE)
- Electrical status in slow wave sleep (ESES)

**Sleep deprivation**
- Juvenile myoclonic epilepsy

Use in polysomnography
Centro-temporal discharges in benign Rolandic epilepsy
Deep NREM sleep

REM sleep

ESES: electrical status epilepticus during slow sleep
Effects of epilepsy on sleep
(varies with type of seizure disorder)
A. Direct effects of epilepsy (severe forms)

Total sleep time reduced

Sleep architecture disrupted with frequent brief arousals (‘fragmentation’)

Quality of sleep and restorative value impaired

Daytime function affected
B. Indirect effects of epilepsy

Anti-epileptic drugs

Better seizure control improves sleep

Harmful effects of AEDs

- Phenytoin (insomnia)
- Barbiturates (oversedation)
- Benzodiazepines (oversedation, respiratory depression, OSA)
- Valproate (weight gain, OSA)

Newer AEDs have less detrimental effects on sleep

Sleep disturbance caused by psycho-social consequences of epilepsy (anxiety, depression)
Sleep disturbances in children with epilepsy
Surveys of sleep disturbances

**Limited studies**

- Mainly adults
- Small scale
- Mixed epilepsies
- Varied assessments, diagnostic categories (mixed sleep problems and disorders) and standards
- Comorbidity?
Overall impressions

**Excessive sleepiness** common (non-restorative sleep from sleep fragmentation, OSA, periodic limb movement disorder)

**Insomnia** common (poorly investigated)

**Non-epileptic parasomnias** can co-exist with epilepsy (may be difficult to distinguish)

Risk of **misdiagnosis** and inappropriate treatment
Aetiology of sleep problems in children with epilepsy

Parenting practices

Difficulty learning good sleep habits
(range of intellectual impairment)

Comorbidities (medical, psychiatric)

Medication effects
Parenting practices (as in other children)

Lack of consistent routine

Poor limit setting

Inadvertent reinforcement
Epilepsy comorbidities likely to contribute to sleep disturbance

Medical
   Neurodevelopmental disorders

Psychiatric disorders
   Anxiety states
   Depression
   Conduct disorder
   Attention deficit hyperactivity disorder (ADHD)
   Autistic spectrum disorders (ASD)
Sleep Disturbance in Children and Adolescents with Disorders of Development: its Significance and Management

Edited by Gregory Stores and Luci Wiggs
Medication in addition to AEDs as a possible cause of children’s sleep problems

**Insomnia**
- Stimulants for ADHD
- Decongestants (pseudoephadrine)
- Bronchodilators (theophylline)
- Beta antagonist antihypertensive agents (propanalol)
- Analgesics (NSAIDs)
- Some antidepressants

**Excessive sleepiness**
- Sedatives-hypnotics (benzodiazepines, antihistamines)
- Major tranquillisers

**Parasomnias** (eg sleepwalking)
- Some hypnotics eg zolpidem
- Some antidepressants
Diagnostic confusions
A. Sleep disorders confused with epilepsy

Non-epileptic parasomnias

- Arousal disorders (sleepwalking, sleep terrors, confusional arousals)
- Rhythmic movement disorders
- REM sleep behaviour disorder
- Nocturnal panic attacks
- Pseudo-parasomnias

Other sleep disorders

- Narcolepsy +/- cataplexy
B. Epilepsies confused with sleep disorders

Benign childhood epilepsies closely related to sleep

Benign Rolandic epilepsy (hemifacial sensorimotor seizures, oropharyngolaryngeal dysaesthesia, speech arrest)

Panayiotopoulos syndrome (focal autonomic seizures)

Late onset occipital epilepsy (visual hallucinations, blindness)

Benign seizures with affective symptoms (terror, screaming)

Nocturnal frontal lobe epilepsy
## Nocturnal frontal lobe epilepsy

### Movements
- Kicking
- Hitting
- Rocking
- Thrashing
- Cycling or scissor movements

### Vocalisations
- Grunting
- Muttering
- Moaning
- Shouting
- Screaming
- Roaring

### Other presentations (inc ‘episodic nocturnal wandering’)

### EEG unhelpful
L prefrontal seizure source
C. Epilepsy and OSA

Co-incidence likely: both common in neurodevelopmental disorders

OSA can trigger epilepsy and also non-epileptic parasomnias (esp arousal disorders)

Treatment of OSA can improve seizures and non-epileptic parasomnias

Consider OSA if poor seizure control or if parasomnias are resistant to treatment
Assessment

Sleep problem may not have come to light

Screening for symptoms and signs

Diagnosis of sleep disorder
Sleep problem may not have come to light

Parents lack basic knowledge about sleep

Even severe sleep problems not reported to GP

Overlooked by clinicians

Importance of screening
Routine screening for sleep problems

History taking

- Bedtime difficulties or problems falling asleep
- Breathing difficulties while asleep
- Waking in the night
- Unusual behaviour, experiences or movements at night
- Difficulty waking up in the morning
- Sleepy or ‘overtired’ during the day
The Children’s Sleep Habits Questionnaire
(completed by parents)

Versions for toddlers-preschool and school-age children

Measures

Bedtime resistance problems          Anxiety about sleep
Wakings during the night             Sleep-disordered breathing
Difficulty getting to sleep          Parasomnias
Short duration sleep                 Daytime sleepiness

Satisfactory psychometric properties

For all children inc those with developmental delay
Diagnosis of sleep disorder

**History** (from parents and others)
- Precise description of sleep problem
- 24-hour sleep–wake pattern
- Developmental history (medical, psychological)
- Family history
- Family circumstances

**Examination**
- Physical
- Behaviour

**Further assessments**
- Questionnaires
- Diaries
- Sleep studies (polysomnography, actigraphy)

**Referral to sleep clinic?**
Treatment
Management of children’s sleep disorders

General principles
- Education for parents and children
- Sleep hygiene
- Treat any underlying disorder

Behavioural methods

Pharmacological
- Hypnotics
- Melatonin
- Stimulants
- Other eg dopaminergic agents or iron supplements for RLS/PLMD

Other
- Chronotherapy (sleep/wake cycle disorders)
- Physical (adenotonsillectomy or CPAP for OSA)
Sleep hygiene

Environment (temperature, noise level, light, bedding)

Regular sleep-wake scheduling (napping, bed time)

Parental sleep practices (routines, relaxation, self-soothing, limit-setting, associations)

Physiological factors (stimulants, fluids, exercise)
Behavioural treatments (mainly for insomnia)

Extinction

Graduated extinction

Faded bedtime

Scheduled waking
Melatonin

Actions
- Hypnotic
- Circadian sleep-wake cycle

Forms
- Immediate release (settling problems)
- Sustained release (night waking)

Evidence
- Mixed (best for neurodevelopmental disorders?)
- Combined behavioural methods and drug treatment?

Uncertainties
- Dosage
- Adverse effects
- Long-term efficacy
Treatment implications in children with epilepsy

Combined epilepsy-sleep approach important

Treatment of epilepsy should lead to improved sleep

Treatment of sleep disorders should improve seizure control

Both can improve wellbeing of the child and the family
Main points

Sleep and epilepsy are connected in many ways

Children with epilepsy are predisposed to sleep disorders

Screening for sleep disorder should be routine

Accurate diagnosis of sleep disorders is essential for treatment purposes and to avoid misdiagnosis

Beneficial effects of combined approach to epilepsy and sleep problems

Research possibilities