Sleep and Moebius Syndrome

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Introduction to sleep
What is sleep?
Typical Sleep Cycle

- **Awake**: Low voltage, high frequency
- **Stage 1 sleep**: Low voltage, mixed frequency
- **Stage 2 sleep**: Sleep spindles, K complexes
- **Stage 3 sleep**: Mostly slow waves
- **Stage 4 sleep**: Slow waves
- **REM sleep**: Rapid eye movement

- Time of Sleep: 0 to 8 hours
Effects of loss of sleep

• Studied more in adults—ethical questions about depriving children of sleep!
• Worse performance than non-sleep deprived on tests of the following:
  – Memory
  – Sustained attention
  – Mood
How does children’s sleep develop?
Overview of sleep

• We’re all born knowing how to sleep
• But how we sleep develops over time due to learned behaviors and changes in our brains
• Sleep develops in 3 key streams:
  – Duration
  – Continuity
  – Day/night cycles
From newborn to grade school

Newborn
• Sleep 16-20 hours per day total
• Sleep for 1-4 hours at a time, then wake for 1-2 hours at a time
• Sleep as much during the day as at night

6-12 year olds
• Sleep 10-11 hours per night
• Consolidated nighttime sleep
• Not typically sleepy during the day
Caveat

• The data we have about average sleep needs, for example, is the product of experience with typically developing children

• We don’t know what is average for children with other medical or neurologic conditions
Sleep problems
Kinds of sleep disorders

- Insomnia
- Sleep related breathing disorders
- Hypersomnias of central origin
- Circadian rhythm sleep disorders
- Parasomnias
- Sleep related movement disorders
- Isolated symptoms, apparently normal variants, unresolved issues, “other”
Insomnia

- Its formal definition involves persistent sleep problems in the face of adequate opportunity for sleep and adverse daytime consequences
- Can refer to difficulty falling asleep, difficulty staying asleep, or both
- The most common sleep problem for children with ASD

-ICSD-2; Johnson and Malow, 2008
Behavioral insomnias of childhood

• Sleep onset association disorder
  – Child falls asleep with parent present, associating presence with falling asleep
  – Parent’s presence required to fall asleep, and back to sleep
  – Everyone wakes multiple times during the night, but not being able to self-soothe brings normal night wakings to attention: often this plays out as complaints of multiple night wakings
Obstructive sleep apnea (OSA)

- Usually associated with snoring
- Repeated, reversible blockages in airflow throughout sleep
- Result in oxygen desaturations, carbon dioxide retention, sleep fragmentation
- Treatable
Obstructive sleep apnea (OSA)

- **Open airway**: where air flows normally (unobstructed breathing)
- **Blocked airway**: where there is no airflow (during an apnea)
Obstructive sleep apnea (OSA)

Children
- Snoring, but many snore and do not have OSA
- Wired
- Attention and behavior problems

- First line treatment is often surgery

Adults
- Snoring, and many who snore have OSA
- Tired
- High blood pressure
- In severe OSA, more cardiovascular complications

- First line treatment is often CPAP
Narcolepsy

• Neurologic disorder of sleep state instability
  – Excessive daytime sleepiness
  – Fragmented nighttime sleep
  – Intrusion of REM characteristics into other phases
    • Muscle atonia into wake: cataplexy, sleep paralysis
    • Vivid dreams into wake: hypnogogic and hypnopompic hallucinations

• Prevalence
  – 0.05% in U.S. adults
  – Unknown in children

Ohayon et al., J Psychosomatic Res, 2005
Stores, Dev Med & Child Neuro, 2006
Cataplexy

- Acute onset muscle weakness, usually transient
- A distinctive feature of narcolepsy, though not necessary for diagnosis
- Often triggered by emotion or laughter
- No alteration of consciousness
- No amnesia for event
- Short duration

Tyagi & Harrington, J Neurol, 2003
Narcolepsy

- Prevalence in U.S. is 1/2,000
- Usually diagnosed in teens or young adults
- Surveys of people with narcolepsy suggest that about 15% had symptoms before age 10, 4.5% before age 5 years
- Potential misdiagnosis with epilepsy based on unresponsiveness due to sleepiness, cataplexy
Diagnosis of Narcolepsy

• History and physical exam
• Overnight sleep study + multiple sleep latency test
  – Mean sleep latency for naps ≤ 8 minutes
  – 2+ sleep onset REM periods during naps
  – Normal values in children, speed of entry into REM sleep, may be different than adults
• Certain HLA types (autoimmune markers) are more strongly associated with narcolepsy
Parasomnias

- Undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousal from sleep
- Can involve skeletal motor and/or autonomic nervous systems

ICSD-3
Schenk, Boyd, & Mahowald, *Sleep*, 1997
Awake
REM
NREM 1-2
NREM 3-4

Partial arousals
Non-REM Parasomnias

• Disorders of arousal
  – Sleepwalking (prevalence up to 17%)
  – Confusional arousals (also up to 17%)
  – Sleep terrors (1-6%)

• Common features
  – Misperception, unresponsiveness, automatic behavior, retrograde amnesia

• EEG signs of sleep during apparent wakefulness

• Patients are generally not sleepy during the day
Parasomnia triggers

- Sleep deprivation
- Being off routine
- Fever and illness
- Antihistamines, neuroleptics, sedatives
- Other sleep disruptors
  - obstructive sleep apnea
  - periodic limb movements)
Parasomnia treatment

- Secure the environment
- Regular sleep wake schedule
- Trial of sleep extension
- Discourage parents from waking
- Avoidance
  - Antihistamines
  - Night-time stimulants
- Benzodiazepenes
REM parasomnias

• REM sleep behavior disorder
  – Rare but possible—in general
  – May be associated with pediatric neurologic disorders

• Nightmares
  – At least occasional in 30-90% of children
  – Increased prevalence in children with anxiety

• Mason and Pack, *Sleep*, 2007
Sleep in Moebius syndrome
Sleep in Moebius syndrome

• Multiple sleep disorders associated
• Possible connection with narcolepsy

# Sleep in Moebius syndrome

Table 2: Subjective complaints of sleep problems in 19 subjects with the Moebius syndrome. Reports from parents or carers in nine children aged 2–11 and self-reports from 10 adults aged 18–48

<table>
<thead>
<tr>
<th>Moebius syndrome subjective complaint of sleep disorder</th>
<th>Affected</th>
<th>Not affected</th>
<th>Normal subjects*</th>
<th>Narcoleptic subjects*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total subject number</td>
<td>19</td>
<td>188</td>
<td>183</td>
<td></td>
</tr>
<tr>
<td>Age (range)</td>
<td>14 ± 13 (2–48)</td>
<td>49 ± 16 (10–79)</td>
<td>54 ± 15 (12–85)</td>
<td></td>
</tr>
<tr>
<td>Sex distribution M:F</td>
<td>9:10</td>
<td>82:106</td>
<td>88:95</td>
<td></td>
</tr>
<tr>
<td>ESS (score range 0–24)</td>
<td>13 ± 3 (n = 5)</td>
<td>7 ± 5 (n = 14)</td>
<td>5 ± 3</td>
<td>20 ± 3</td>
</tr>
<tr>
<td>Insomnia score (0–100)</td>
<td>74 ± 19 (n = 10)</td>
<td>28 ± 25 (n = 7)</td>
<td>28 ± 24</td>
<td>43 ± 29</td>
</tr>
<tr>
<td>Fall with laughter (atonia scale score 0–200)</td>
<td>92 ± 7 (n = 4)</td>
<td>3 ± 11 (n = 15)</td>
<td>7 ± 8</td>
<td>128 ± 27</td>
</tr>
<tr>
<td>Parasomnias (score 0–10)</td>
<td>4 ± 12 (n = 19)</td>
<td>2 ± 2</td>
<td>5 ± 3</td>
<td></td>
</tr>
</tbody>
</table>

*Data from King’s/Maudsley sleep disorders clinic and controls. Scales not validated in children with learning difficulty (Chen et al. 1995).
1 Modified ESS score using items 1–6 only from 8 item score system. Results corrected for total score 24. 2 Insomnia score rating scale 0–100, sleep quality excellent–awful. Data lacking in two Moebius subjects. 3 Data from propensity to fall with laughter score, range 0–200. 4 Parasomnia score: presence or absence of ‘excess’ specified parasomnias in comparison with non-Moebius sibs of similar age.

Affection status: defined as positive or negative response to the following questions: do you have excess daytime sleepiness?; do you have very poor or disturbed night sleep?; do you fall down with laughter?; do you have frequent or severe sleep talking, walking, muscle jerking, body restlessness or snoring during night sleep? All scores: mean ± SD. No statistical comparisons made in view of different reporting source, origin, and age of separate subject groups. Mean ± SD (range, median). Night sleep score: excellent–awful, 0–100. Day sleep score: modified ESS omitting items 7 and 8; total 6 item score 0–18 × 24/18. Atonia rating scale derived from items 1 and 2 of cataplexy rating scale; score range 0–200.

### Parasomnias

<table>
<thead>
<tr>
<th>Type of parasomnia</th>
<th>N=19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleeptalking</td>
<td>13</td>
</tr>
<tr>
<td>Sleep jerking, restlessness, sleepwalking</td>
<td>12</td>
</tr>
<tr>
<td>Sleep sweating</td>
<td>7</td>
</tr>
<tr>
<td>Snoring</td>
<td>6</td>
</tr>
<tr>
<td>Breath holding</td>
<td>1</td>
</tr>
</tbody>
</table>

Parasomnias

- Report of 33 cases of “parasomnia overlap syndrome” involving sleepwalking, sleep terrors, and REM sleep behavior disorder
  - 11 symptomatic (as opposed to idiopathic)
  - 1 of these was a patient with Moebius syndrome

- Schenck, Boyd, & Mahowald, *Sleep*, 1997
Brainstem abnormalities

• Congenital central hypoventilation case reports—one source mentions around 15 case reports in the literature
• Hypoventilation worse during sleep than wakefulness, with low oxygen and high CO$_2$

Nunes et al., *Arq Neuropsiquiatr*, 1999
Sleep disordered breathing

• People with Moebius syndrome may be predisposed to sleep disordered breathing
• Groups of respiratory neurons are near cranial nerves VI and VII
• Craniofacial differences may contribute to obstruction
• Limitations on tongue range of movement or function could contribute to obstruction during sleep

• Gilmore et al., *J Child Neurol*, 1991
REM behavior disorder

• Case reports in Moebius syndrome in adults and children thought to be associated with structural brainstem lesions

• Anderson, Shneerson, & Smith, *J Neurol Neurosurg Psychiatry*, 2007
• Lloyd et al., *J Clin Sleep Med*, 2012
Narcolepsy

- Diagnosis can be challenging as identification of REM sleep is more difficult because of limited eye movements
- If narcolepsy is present, again, it may be structural due to brainstem changes

- Parkes, J Sleep Res, 1999
Cataplexy

- Several case reports of cataplexy in people with Moebius syndrome, including isolated symptomatic cataplexy (without other symptoms of narcolepsy)
- No relationship with HLA typing specific to narcolepsy

Tyagi & Harrington, *J Neurol*, 2003
Light sensitivity?

- Light is a powerful signal about when to be alert
- Do people with Moebius tend to avoid bright light?
Autism spectrum disorder (ASD) and sleep

- Sleep problems are common among typically developing children
- Sleep problems are also common among children with ASD
- Souders et al. (2009) found 45% of parents of typically developing children and 66% of parents of children with ASD reported sleep problems
- Actigraphy data showed a similar prevalence of sleep disturbance among the 2 groups, particularly for increased sleep latency
ASD and sleep

• The most common sleep problems in children with ASD include difficulties with falling asleep (sleep onset) and staying asleep (sleep maintenance)

• Children with problems falling asleep were “taking a long time to wind down,” “replaying cartoons in their heads or talking incessantly,” “anxious and scared of the dark or of seeing insects in their beds”

• Not all children with autism are bad sleepers!

  • Malow et al., 2006
ASD: factors that affect sleep

- Anxiety
- Compulsive behaviors
- Sensory sensitivities
- Need for routine
- Alerting side effects of medications
- Lack of attention to social cues
- Difficulties with self-regulation
Diagnosis
Clinic visit

• Sleep medicine subspecialty evaluation, typically with a physician or psychologist, includes sleep-focused history, physical, and neurological examination; review of relevant records, including sleep questionnaires and diaries

• Recommendations for additional testing, behavior management, medical management
# Child's Sleep Habits

**Child's Sleep Habits**  
(Preschool and School-Aged)

The following statements are about your child's sleep habits and possible difficulties with sleep. Think about the past week in your child's life when answering the questions. If last week was unusual for a specific reason (such as your child had an ear infection and did not sleep well or the TV set was broken), choose the most recent typical week. Answer USUALLY if something occurs 5 or more times in a week; answer SOMETIMES if it occurs 2-4 times in a week; answer RARELY if something occurs never or 1 time during a week. Also, please indicate whether or not the sleep habit is a problem by circling “Yes,” “No,” or “Not applicable (N/A).”

## Bedtime

Write in child's bedtime: ____________

<table>
<thead>
<tr>
<th></th>
<th>3 Usually (5-7)</th>
<th>2 Sometimes (2-4)</th>
<th>1 Rarely (0-1)</th>
<th>Problem?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child goes to bed at the same time at night</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child falls asleep within 20 minutes after going to bed</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child falls asleep alone in own bed</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child falls asleep in parent's or sibling's bed</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child falls asleep with rocking or rhythmic movements</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child needs special object to fall asleep (doll, special blanket, etc.)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child needs parent in the room to fall asleep</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child is ready to go to bed at bedtime</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child resists going to bed at bedtime</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child struggles at bedtime (cries, refuses to stay in bed, etc.)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
<tr>
<td>Child is afraid of sleeping in the dark</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>Yes No N/A</td>
</tr>
</tbody>
</table>

Owens et al., *Sleep,* 2000
Treatment

• Behavioral and environmental modifications
  – Bedtime routine
  – Controlling light exposure
  – Preventing or gradually fading sleep associations
• Melatonin
• Addressing disruptive behaviors, medical and other disorders
• Surgery or positive airway pressure (PAP) for obstructive sleep apnea
• Medications
How to promote good sleep

• Regular bedtime routine
  – Calming, wind-down activities
  – Bedtime stories!
• Consistent schedule for bedtime and wake time
• Limit caffeine
  – None at least 3-4 hours before bedtime!
• Keep electronics out of the bedroom
• Daily exercise
Optimal environment for sleep

• Quiet
  – Sometimes white noise (such as from a fan) helps
• Dark
  – Nightlight OK
• Cool
  – < 75 degrees
• Comfortable
• No electronics!
Is it time for more research?

Survey via Moebius Syndrome Foundation support groups looking at larger numbers for prevalence of sleep problems?