Sleep Problems In Adults With Neurodevelopmental Disorders

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I have no conflicts of interest related to this talk and subject
Overview of Talk

- Sleep disorders are common in adults with neurodevelopmental disorders with/without concomitant intellectual disability (ID), autism spectrum disorder (ASD), and/or attention deficit/hyperactivity disorder (ADHD);
- Screening tools for identifying sleep problems in adults with NDD;
- Evaluating and treating insomnia in adults with NDD.
NDDs are group of disorders caused by changes in early brain development → cognitive and behavioral changes in motor, sensory, speech and/or language systems.

NDDs 1-2% of general population.

NDDs often associated with intellectual disabilities (IDs), attention deficit/hyperactivity disorder (ADHD) and/or autism spectrum disorder (ASD).
Sleep and Neurodevelopment Disorders Often Are Poor Bedfellows

- Sleep problems are common and often persistent in people with NDDs, ID, ADD/ADHD, and/or ASD;
- Complex relationships often bidirectional between sleep problems, problematic behaviors, cognitive function and learning in such individuals.
Deficits Vary in Individuals with Neurodevelopmental Disorders

- Sleep (or lack of it) impact upon all of these.
Sleep Disorders in Adults with NDD Same as Those Seen in Neurotypical Adults

Difficulty falling asleep
Difficulty staying asleep
Early morning awakenings
Unrefreshing Sleep
Daytime sleepiness
Suspected sleep apnea
Reversals of sleep/wake timing
Parasomnias

However, sleep problems in people with NDD compared to general population are:

- More Common
- More Frequent
- More Persistent
- More Severe
Sleep Disturbances **Common** in Adults with NDD, ID, ASD, and/or ADHD

**Study #1**: Sleep/wake complaints among 205 community-living adults with ID:
- 27% Difficulty falling asleep;
- 56% Nocturnal awakenings;
- 15% Sleep disordered breathing.

- Insomnia (difficulty falling or staying asleep) most common complaint.

Adults with HF-ASD had significantly more general sleep disturbances compared to NT:

- HF-ASD more likely to meet criteria for insomnia (28% HF-ASD vs 6% NT);

HF-ASD adults had:

1) Higher scores on validated sleep questionnaire (PSQI);
2) Longer time to fall asleep (sleep latency) on actigraphy;
3) Poorer sleep efficiency, more fragmented sleep, and longer sleep latency on sleep diary.

Case-control cross-sectional study of 36 adults with HF-ASD and 36 age, IQ- and sex-matched neurotypical (NT) adults.

Study #3: 164 (111 M, 53 F) adults with NDDs attending ASD and ADHD clinics:
- 111 M, 53 F, 30 ASD, 98 ADHD, 34 ASD+ADHD;
- 91% had poor sleep on Pittsburgh Sleep Quality Index (total score 5+);
- 44% moderate/severe insomnia on Insomnia Severity Index (score 15+).

1) High insomnia scores correlated with high anxiety scores (not depression);
2) High anxiety scores correlated with hyperactivity (not inattention);
3) Anxiety scores higher in ASD.
### Case-Control PSG Studies Find Poorer Sleep Architecture More Often HF-ASD than NT Adults

<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Sample Size</th>
<th>PSG Findings</th>
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</thead>
<tbody>
<tr>
<td><strong>Study #1</strong> Limoges et al. 2005</td>
<td>27 adolescents and adults (16-27) with HF-ASD and 78 NT adults</td>
<td>HF-ASD longer sleep onset latency, more nocturnal awakenings, and poorer sleep efficiency</td>
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<td><strong>Study #2</strong> Tani et al. 2003</td>
<td>20 adults with HF-ASD and 10 NT adults</td>
<td>Higher percent of HF-ASD had wake after sleep onset &gt; 30 min compared to NT adults.</td>
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<td><strong>Study #3</strong> Hare et al. 2006</td>
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Some NDDs Have Sleep Problems So Prevalent To Be Considered Behavioral Phenotype

- Smith-Magenis Syndrome
- Rett Syndrome
- Down Syndrome
- Autistic Spectrum Disorder
- Williams Syndrome
- Fragile X Syndrome
- Prader-Willi Syndrome
Smith-Magenis Syndrome (SMS)

Fig. 1 Typical SMS phenotype with ‘tent’ upper lip and depressed nasal bridge a, b, c, d. Brachydactyly a, b. Young adults SMS often present with synophris (d, e) and prognatism d. Wounds from skin picking can be seen at any age d

Behavioral disturbance and treatment strategies in Smith-Magenis syndrome
Alain Poisson1,2,3, Alain Nicolas1,2, Pierre Coche4,5, Damien Sanfelice5, Caroline Jigot6, Hélène de Lenczydne, Patrick Francois3, Vincent Des Portes2, Patrick Eloy7,8 and Caroline Demly9,10

Abstract

Background: Smith-Magenis syndrome is a complex neurodevelopmental disorder that includes intellectual disabilities, speech delay, behavioral disturbance, and typical sleep disorders. Ninety percent of the cases are due to a 17p11.2 deletion encompassing the ZNF469 gene. Other cases are linked to mutations of the same gene. Behavioral disorders often include autism, attention deficit/hyperactivity disorder, self-injury with amputolobotomy, and polymicrogyria (abnormal folding of brain folds) among others. Interestingly, the stronger the speech delay and sleep disorders, the more severe the behavioral issues. Sleep disturbances associate excessive daytime sleepiness with nighttime hyperactivity. They are underpinned by an inversion of the melatonin secretion cycle. However, the combined intake of beta-blockers in the morning and melatonin in the evening may radically alleviate the circadian rhythm perturbations.

Discussion: Once sleep disorders are treated, the next challenge is finding an effective treatment for the remaining behavioral problems. Unfortunately, there is a lack of objective guidelines. A comprehensive evaluation of such disorders should include sleep disorders, potential causes of pain, neurocognitive level and environment (e.g., family and school). In any case, efforts should focus on improving communication skills, identifying and treating attention deficit/hyperactivity, aggression and anxiety.

Summary: Treatment of Smith-Magenis syndrome is complex and requires a multidisciplinary team including, among others, genetics, psychologists, neuropediatricians/neurologists, somatologists, developmental and behavioral pediatricians, and speech and language therapists.
Smith-Magenis Syndrome (SMS)

- Characterized by developmental delay with IQ 40s to 60s, short stature, hoarse deep voice, obesity, scoliosis, distinctive facies and peripheral neuropathy;
- SMS mutation or small interstitial deletion in a crucial transcriptional regulator gene of circadian clock on chromosome 17;
- Circadian rhythm disorders in SMS thought related to disturbed regulation of downstream circadian clock genes;
- 96% of SMS children have inverted endogenous melatonin secretion, peaking in day rather than night;
- Oral acebutolol (b1-adrenergic antagonist, 10 mg/kg) given in morning coupled with evening dose of melatonin improved sleep/wake complaints.
- Cognitive behavior insomnia treatments also needed. Screen for symptoms of OSA given midface hypoplasia, obesity and scoliosis.
People with Prader-Willi Syndrome (PWS) Often Have Sleep Disordered Breathing but Also Central Hypersomnia

- Severe central hypotonia at birth with a poor suck, weak cry, lethargy, and decreased movement during infancy
- Delayed language development
- Delayed motor milestones
- Characteristic facies (almond-shaped eyes, strabismus, narrow bifrontal diameter, thin upper lip, down-turned mouth)
- Small hands and feet
- Short stature
- Hyperphagia and insatiable appetite by age of 1 to 6 years, morbid obesity by age of 4 years
- Fat storage in the abdomen, buttocks, and thighs even in nonobese patient
- Hypothalamic hypogonadism (genital hypoplasia, incomplete pubertal development, and, in most cases, infertility)
- Stubbornness, temper tantrums, self-injury, skin-picking, food foraging, impulsivity, mood lability, repetitive speech
- Learning difficulties, poor academic performance, mean IQ 60s to 70s
- Impaired social cognition, literal-mindedness, cognitive inflexibility
- Sleep-disordered breathing (especially sleep-related hypoventilation, often mild obstructive sleep apnea)
- Hypothalamic dysfunction with central hypersomnia
- Impaired growth hormone secretion and low serum insulin-like growth factor-1 levels
Children and adults with DM1 at risk for:
- Obstructive and central sleep apnea;
- Central hypersomnia;
- Cognitive impairment making PAP adherence challenging;
- Hypothyroidism;
- Cardiac conduction disorder (60-times general population).
Evaluating and Treating Some Common Sleep Disorders Seen in Adults with NDD
Many Sleep Problems in Adults with NDD Can Be Treated with Teamwork

- Insomnia;
- Circadian rhythm disorders;
- Sleep apnea
- Central hypersomnia
- At least once a year screen individual for sleep problems, if positive for possible insomnia, then;
- Request patient (and/or caregiver) to complete a 2-week daily sleep log (and teach them how to do it);
- Ask them to calculate (if possible) their sleep efficiency (how much time in bed spent sleeping).

Screening Tools For Identifying Sleep Disorders In Adults With Neurodevelopmental Disorders
Instruments We Use to Study Sleep Disorders in People with NDD

- Sleep questionnaires
- Sleep diary
- Actigraphy
- In-lab Polysomnography
- Home Sleep Apnea Test

Sleep Quality Assessment (PSQI)

What is PSQI, and what is it measuring?
The Pittsburgh Sleep Quality Index (PSQI) is an effective instrument used to measure the quality and patterns of sleep in adults. It differentiates "poor" from "good" sleep quality by measuring seven areas (components): subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction over the last month.

INSTRUCTIONS:
The following questions relate to your usual sleep habits during the past month. Please answer all questions.

During the past month,

1. When have you usually gone to bed?
2. How long (in minutes) has it taken you to fall asleep each night?
3. What time have you usually woken up in the morning?
4. How many hours of actual sleep did you get at night?
5. If you have a partner, how many hours of sleep did the other person get at night?

Scoring:

Add the seven component scores together. A total score of 8 or greater is indicative of poor sleep quality.

If you scored 9 or more it is suggested that you discuss your sleep habits with a healthcare provider.
Self-Reported Sleepiness Scales

Abnormal ESS score >10.

It is virtually impossible to treat insomnia or circadian rhythm diary without a sleep diary;

Actigraphy can help but still need a diary;

Inability to complete a diary a measure of willingness to pursue treatment.

Can use sleep apps (Sleep Cycle or Sleep Bot)
• Obstructive sleep apnea (OSA) is probably only sleep disorder in which a sleep diary not so helpful.
Screening Tools for Obstructive Sleep Apnea (OSA) in Adults with NDD

GASP Screen for OSA

- During the night do you?
  - G gasp or choke?
  - A stop breathing?
  - S snore loudly
  - P perspire (sweat);
- Do you have trouble sleeping?
- Is your sleep refreshing?
- Are you sleepy in the day?
- Take naps?

Stop-Bang Questionnaire

1. Snoring
   Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
   - Yes/No
2. Tired
   Do you often feel tired, fatigued, or sleepy during daytime?
   - Yes/No
3. Observed apnea
   Has anyone observed you stop breathing during your sleep?
   - Yes/No
4. Blood pressure
   Do you have or are you treated for high blood pressure?
   - Yes/No
5. BMI more than 35 kg/m²?
   - Yes/No
6. Age
   Age over 50 yr old?
   - Yes/No
7. Neck circumference
   Neck circumference greater than 40 cm?
   - Yes/No
8. Gender
   Gender male?
   - Yes/No

High risk of OSA: answering yes to three or more items
Low risk of OSA: answering yes to fewer than three items
## Stop-Bang Questionnaire Screening for Obstructive Sleep Apnea in Adults

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Treating Insomnia in People with Neurodevelopmental Disorders
Insomnia in Adults with NDDs Began in Childhood and Have Persisted
Clinical features of insomnia:
- Trouble falling asleep (>30 minutes);
- Frequent and/or prolonged nocturnal awakenings;
- Early morning awakenings with difficulty returning to sleep;
- Poor sleep quality;
- Poor sleep efficiency;
- Cognitive arousal;

Severity of insomnia judged by:
- Frequency, intensity and duration of sleep difficulties;
- Impact on daytime functioning, mood and quality of life.

Cultural issues of insomnia:
- How long to sleep at night and/or to nap;
- Is insomnia a disease, complaint, disorder, symptom, and/or finding;
- Is insomnia due to physical and psychiatric problems, too much work, exhaustion,
Most Common Sleep Problems in Adults with NDD, ID and/or ASD

- Difficulty falling and/or staying asleep;
- Frequent nocturnal awakenings;
- Early morning awakenings;
- Too much time in bed not sleeping;
- Long daytime naps; day/night reversal;
- Impairments in daytime arousal and vigilance;
- Meltdowns and behavior problems exacerbated by insufficient sleep/sleepiness;
- Impaired circadian (biologic) clock rhythms.
Inability to benefit from social or communicative cues about sleep

Repetitive thoughts/behaviors at bedtime interfere with settling

Hyperarousal or difficulty with self-regulation

Hypersensitivity to environmental stimuli

Unhealthy sleep practices and patterns

Neurobehavior Factors Which Can Contribute to Insomnia in NDD
Factors Which Can Contribute to Insomnia in Adults with NDD and/or ID

- **Intrinsic abnormalities of sleep regulation**
  - Melatonin, growth hormone, oxytocin, ferritin, clock gene mutations, hypothalamic dysfunction, central hypersomnias

- **Comorbid medical conditions**
  - Epilepsy, pain, asthma, eczema, GERD, sensory deficits, physical deformities, developmental delay, learning disabilities, communication difficulties

- **Psychiatric comorbidities**
  - Anxiety, depression, PTSD, hallucinations, psychosis

- **Medication effects**
  - Stimulants, sedatives, antipsychotics, antidepressant, antiepileptics

- **Primary sleep disorders**
  - Sleep apnea, hypoventilation, hypoxemia, RLS, parasomnias, insomnia, circadian rhythm disorders
Strategies to Improve Insomnia in Adults with Neurodevelopmental Disorders

- **Stimulus control therapy** (view bed and bedroom as a sleep stimulus);

- **Sleep restriction** (restrict time spent in bed to consolidate sleep and enhance sleep quality);

- **Relaxation training** (decrease arousal and anxiety)

- **Circadian rhythm entrainment** (reinforce or reset circadian biologic clock using chronotherapy and/or light)

- **Cognitive behavior therapy** (combination of behavioral and cognitive therapies listed above).

- Level of intellectual functioning and motivation in patient (and caregivers) influence treatment choices and possibilities.
Range of Treatment Strategies for Insomnia in Adults with NDDs

- Motivation and degree of intellectual impairment;
- Willingness of patient, caregivers, and/or staff influence choices;
- However, can succeed if pursued.

Optimal scheduling;
Stimulus control;
Sleep Hygiene;
Relaxation exercise;
Imagery;
Light therapy.

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Goal: Efficient Consolidated Sleep

Avoid sleep deprivation when trying to improve bedtime schedules.

Modify bedtimes by progressive adjustment of bed and daytime napping to achieve most efficient and consolidate sleep/wake pattern.

Sleep restriction: restrict time in bed (TIB) at night to estimated sleep duration and gradually increasing TIB once patient sleeps thru;

Gradually shorten daytime naps, providing stimulating alternatives to napping;
Stimulus Control Therapy

- Relax before bedtime, avoid going to bed worried or angry; Use bedroom only for sleep (and intimacy);
- Remove all electronic devices from bedroom; Do not read, watch TV, eat or worry in bed;
- Go to bed only when tired and sleepy;
- Get up at same time every morning;
- Do not nap during day and try not to fall asleep anywhere else but in bed;
- If unable to fall asleep within 20 minutes in bed, get up, go to another room with lights dim and do something relaxing sedentary, return to bed when sleepy. If return to bed and again can’t sleep, leave bedroom again; repeat as needed throughout night even after awakenings.
Stimulus Control Therapy Value?

- **Indication**: chronic difficulty falling and/or staying asleep;
- **Rationale**: maladaptive association of bed/bedroom with wakefulness; breakdown of healthy association of bed/bedroom with rapid-onset well-consolidated sleep;
- **Mode of action**: To break the cycle, patient must not spend time wide awake in bed or bedroom; associate bedroom = sleep;
- **Efficacy**: Most effective component of CBT-I; can be effective stand-alone therapy for many insomnia sufferer
## Combating Patient Excuses and Resistance to Stimulus Control

<table>
<thead>
<tr>
<th>Complaint</th>
<th>Responses and Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>If I get up out of bed, I’ll become more alert and sleep even less if I stayed in bed trying to sleep</td>
<td>Less sleep, more drive to sleep next day increasing chance of better sleep next night; Change mindset, acceptance vs. frustration; SCT = establish new conditioned response to set your mind/body for better sleep in long run.</td>
</tr>
<tr>
<td>I want to stay in my warm comfortable bed.</td>
<td>Have a blanket/robe nearby; Plan where you will go and set up with pillows, blankets, candles; what to do there (e.g. watch a particular TV show, magazine, crafts, massage device/heating pad)</td>
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**Sleep Restriction**

- **Determine average total sleep time per 24 hours:**
  - Obtain and review sleep diary (+ actigraphy) to determine average total sleep time (TST) per 24 hours
    - Calculate 24 hour sleep time;
  - **Initial sleep restriction prescription:**
    - Time in Bed (TIB) = Total Sleep Time (TST) + 15 min for 1 week.
    - BUT a minimum TIB of 4-5 hours.

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**Sleep Restriction Instructions**

1. Your bedtime is ____________.

2. Set your alarm and get up at the same time every morning, regardless of how much sleep you got during the night. Your wake time is ____________.

3. Do not nap during the day.*

* In cases where sleepiness might cause harm to self or others, go ahead and nap, go to bed earlier, sleep in, etc. In elderly, scheduling a nap might be beneficial, but try to limit to 30 minutes (and track this!).

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Sleep Restriction Titration Rules

- Based on average of sleep efficiency (SE, percent TIB sleeping) >90%, increase bedtime by 15 minutes;
  - If SE 85-89% same TIB;
  - If SE <85%: decrease time in bed by 15-30 minutes.
  - If elder, increase TIB by 15 minutes if SE >80% and allow 30-minute nap;
- As sleep consolidation improves, time in bed and asleep increases;
- Creates a mild state of sleep deprivation promoting more rapid sleep onset and more efficient sleep.
Sleep Restriction Therapy (SRT)

- **Indication:** difficulty falling/staying asleep;
- **Rationale:** chronic insomnia sufferers unable to get appropriate amount of consolidated sleep at appropriate time of day; can benefit from hard reset of their sleep schedule;
- **Mode of action:** Limit amount of time person can spend in bed to their average sleep time;
- **Efficacy:** very effective, critical component of CBT-I; generally not done alone.
Sleep Hygiene Education

- Avoid caffeine 4-6 hours before bedtime;
- Regular exercise in morning/afternoon; avoid exercise before bedtime;
- Avoid alcohol, nicotine, large/heavy meals, excessive fluid, spicy/acidic foods close to bedtime;
- Create a sleep-friendly environment: dark, cool, quiet bedroom with a comfortable bed;
- Get up same time every morning regardless of amount of sleep obtained; Avoid daytime naps;
- Get exposure to natural light every morning.
Effectiveness of Sleep Hygiene?

- **Rationale:**
  - Chronic insomnia sufferers often overcompensate for lost sleep by engaging in behaviors that over time sabotage their sleep habits;

- **Mode of action:**
  - Bring awareness about habits that contribute to chronic insomnia;
  - Empower person to engage in activities that are healthy and sleep promoting;

- **Effectiveness:**
  - Not effective stand-alone therapy for chronic insomnia, but effective with combined with stimulus control and sleep restriction therapy.
Progressive muscle relaxation
Guided imagery
Diaphragmatic breathing.

**Indication:** insomnia suffers who view their insomnia as “inability to relax”;

**Rationale:** chronic insomnia can arise from overactive sympathetic nervous system with hyperarousal;

**Effectiveness:** effective as adjunct for anxiety-related problems.
- While inhaling, contract one muscle group for 5-10 seconds, then exhale and suddenly release the tension in that muscle group.
- Relax for 10-20 seconds, then move on to the next muscle group.
- While releasing the muscle tension, try to focus on the changes you feel when the muscle group is relaxed. Image release of tension including stressful feelings are flowing out of your body as you relax each muscle group.
- Gradually work your way up the body contracting and relaxing muscle groups.

![Progressive Muscle Relaxation Diagram]
Breathe in slowly for 5 seconds then hold your breath for 5-10 seconds then breathe out for 5-10 seconds;

Repeat until you feel calm;

Pay attention to feeling of air filling your lungs, hold you breath a little longer than an ordinary breath; and pretend you are breathing out through a straw.
Using Visual Imagery to Relax

- Think about some of your favorite and least favorite places.
- Paint a picture of the calming place in your mind: Imagine every little detail. Go through each of your senses and imagine what you would experience in your relaxing place.
- Example: You are on a tropical beach…
  - Sight: Sun high in sky and you’re surrounded by white sand. There’s no one else around. The water is a greenish-blue and waves are calmly rolling in from the ocean.
  - Sound: You can hear the deep pounding and splashing of the waves. There are seagulls somewhere in the background.
  - Touch: The sun is warm on your back, but a breeze cools you down just enough. You can feel sand moving between my toes.
  - Taste: You have a glass of lemonade that’s sweet, tart, and refreshing;
  - Smell: You can smell the fresh ocean air, full of salt and calming aromas.
Nightmare Re-imaging Therapy

- Set aside time next day to think through your nightmare and discuss it with someone;
- Identify worse moment in your nightmare:
  - Where are you? What are you aware of? What is happening?
- What emotions are you feeling at that worst moment?
  - Identify your emotions and what you feel in your body either during the nightmare or after waking up;
- What would you prefer to feel in that moment?
- How would the story need to be changed for you to feel that way.
Sleep Well (And Don’t Let Bed Bugs Bite)
References on Sleep Problems in Adults with Intellectual Disability