

Promoting Sleep in Children with Autism Spectrum Disorders

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Presentation Outline

- What sleep concerns have been reported in children with autism spectrum disorders (ASD)?
- Why are sleep concerns important to treat in children with ASD?
- What are their causes? Neurobiological? Behavioral? How should the evaluation be approached?
- What treatments exist for sleep disturbances in this population?

Sleep Concerns/Disorders in Autism

- ✓ Prevalence of sleep problems is 44-83% (Richdale, 1999)
- ✓ In comparison, approximately 30% of infants and preschool children who are typically developing have sleep problems (Owens, 2000) with the percentage decreasing in school-aged children (Stein, 2001)
- ✓ Sleep concerns occur regardless of IQ. Although the degree of mental retardation tends to predict sleep impairment in most developmental disabilities, IQ does not predict the prevalence or severity of sleep concerns in ASD (Richdale, 1999; Patzold, 1998).

Sleep Concerns in Autism

- Studies using parentally-completed questionnaires and sleep diaries report most common sleep concern is insomnia (difficulty initiating or maintaining sleep):
 - Prolonged time to fall asleep
 - Later bedtime
 - Decreased sleep duration and continuity
 - Increased arousals and awakenings
 - Early morning wake time
- (Hoshino, 1984; Richdale, 1995; Patzold, 1998; Stores, 1998; Hering, 1999; Honomichl, 2002; Wiggs, 2004; Williams, 2004)

Sleep Concerns in Autism

- Apart from insomnia, other sleep concerns reported by parents include:
 - Sleep disordered breathing
 - Bruxism
 - Arousals from sleep with confusion or wandering
 - Rhythmic movement disorder
 - Leg movements
 - Daytime sleepiness

Sleep Concerns are not Universal in Autism

- Only 54% of parents surveyed reported that their child had a sleep problem (Honomichl and Anders, 2002)
- In our cohort of medication-free, seizure-free children ages 4-10 years with normal intelligence, 55% had no or only mild sleep problems according to their parents.
- Why is this important?
- What are some reasons why kids with autism sleep well?
 - ✓ Very lucky parents
 - ✓ Genetics
 - ✓ Parent who is a sleep specialist

Daniel (age 5) and Austin (age 8)



Characterizing Sleep in Children with ASD

- Sleep studies (polysomnography, PSG) have documented REM sleep abnormalities, such as immaturity in the organization of eye movements into discrete bursts, REM sleep without atonia, or features of undifferentiated sleep in which NREM and REM sleep were difficult to distinguish
- We are taking a multidimensional approach to sleep in children with ASD, combining PSG with behavioral data
- Results published to date include 21 children with ASD— 11 poor sleepers and 10 good sleepers— as well as a comparison group of 10 age-comparable typically developing good sleepers

Malow et al, SLEEP, 2006

Sleep in Children with Autism

Why?

Having quality sleep may affect how a child behaves. The goal of our study is to understand sleep patterns in children with autism and typically developing children in relation to daytime behavior.

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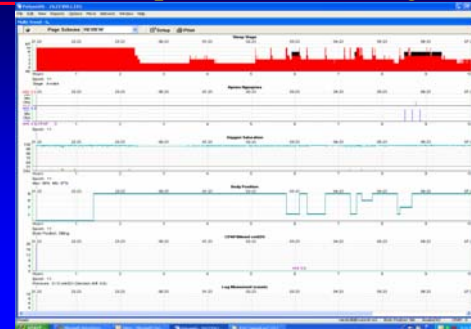
✓How perform PSGs in children with ASD???

- ✓Fun-loving, child friendly experienced sleep techs
- ✓Create picture books to help prepare children for the sleep study experience
- ✓Quiet play activities, stickers, activity books
- ✓Home sleep study or acclimation visit preceding admission to hospital sleep lab

Vanderbilt Study: Sleep and ASD

- Ages 4-10 years, clinical diagnosis of ASD confirmed by Autism Diagnostic Observation Scale (ADOS), no history of mental retardation, epilepsy, and not taking psychotropic medications—10 good sleepers and 11 poor sleepers
- Age comparable group of 10 typically developing children— all good sleepers
- “Good sleep” vs. “Poor sleep” defined by parental report on a parental concerns checklist
- Child Sleep Health Questionnaire (CSHQ) scores on two domains--sleep onset delay and sleep duration-- were significantly worse in ASD poor sleepers as compared to other groups ($p \leq 0.03$)

“Poor sleeper” with ASD: night 1



“Good sleeper” with ASD: night 1



ADOS scores related to sleep concerns

- Compared ADOS results quantitatively across participants. Used algorithm items common to ADOS modules 2 and 3.
- Distribution of autism vs. PDD-NOS was not related to good vs. poor sleep
- Compared to ASD good sleepers, the ASD poor sleepers scored higher (worse) on the reciprocal social interaction items (6.8 ± 1.9 vs. 4.8 ± 1.5 ; $p = 0.047$). The communication and total ADOS scores did not differ between ASD good and poor sleepers.

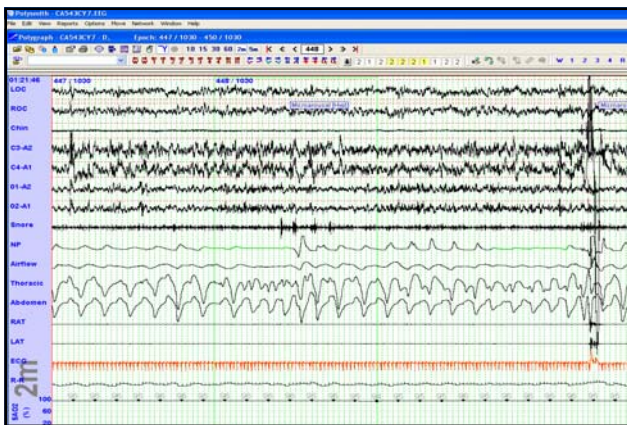
Vanderbilt Sleep and ASD Study: Conclusions

- Parentally reported sleep concerns of insomnia in children with ASD are substantiated by validated sleep questionnaires and by PSG
- Good sleepers with ASD showed fewer affective problems and better social interactions than ASD poor sleepers
- While our data document an association between sleep in ASD and daytime functioning, we cannot determine whether poor sleep is the cause or result of more problematic daytime functioning in ASD, or whether the severity of ASD is contributing to both poor sleep and more impaired daytime functioning
- Interventional studies that improve sleep will be necessary to sort this out

Does improving sleep in ASD affect daytime behavior?

- One child in the ASD poor sleep group with symptoms of sleep-disordered breathing on the CSHQ showed obstructive sleep apnea.
- After tonsillectomy, she exhibited a marked improvement in sleep, daytime behavior, and autism symptomatology.

(Malow et al, *Pediatric Neurology*, 2006)



Child with ASD and sleep apnea

“The change in my daughter has been absolutely remarkable, and I’m hoping the next few months will bring even more improvements. Her interest in everything and everyone around her has greatly increased. She sleeps soundly through the night and wakes happy in the morning...the length of time she can follow directions has increased.”

- ✓ CSHQ domains of restless sleep, sleeping too little, daytime sleepiness, and sleep-disordered breathing normalized
- ✓ CBCL domains of emotional reactivity, social withdrawal, anxiety, and sleep disorder normalized
- ✓ ADOS remained consistent with autism spectrum disorder

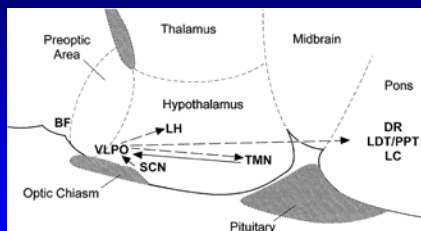
Presentation Outline

- What sleep concerns have been reported in children with autism spectrum disorders (ASD)?
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- **What are their causes? Neurobiological? Behavioral? How should the evaluation be approached?**
- **What treatments exist for sleep disturbances in this population?**

Sleep and Autism are Interrelated: Neurochemistry

- Sleep and autism share similar neurotransmitters
 - ✓ GABA
 - ✓ Serotonin
 - ✓ Melatonin
- These neurotransmitters play a critical role in regulating the sleep-wake cycle
- Aberrations in these systems due to autism may be manifested in impaired control of sleep-wake regulation

Ventrolateral preoptic neurons (VLPO) promote sleep, via GABAergic mechanisms



- ✓ 80% of VLPO neurons contain glutamic acid decarboxylase
- ✓ VLPO neurons increase firing rates during NREM sleep
- ✓ VLPO lesions reduce sleep and EEG slow wave activity

Sleep and Autism are Interrelated: Neurochemistry

- Sleep and autism share similar neurotransmitters
 - ✓ **GABA**
- GABAergic interneurons are disrupted in autism (Levitt, 2004)
- An autism susceptibility region has been identified on chromosome 15 (McCauley and Sutcliffe, 2004)

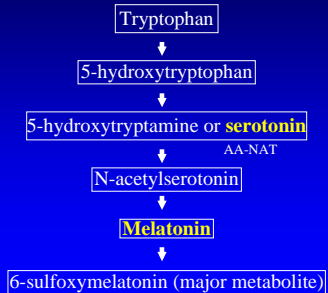
Sleep and Autism are Interrelated: Neurochemistry

- Sleep and autism share similar neurotransmitters
 - ✓ **Serotonin**
- Serotonin may promote sleep by dampening cortical arousal systems, or by stimulating the accumulation of hypothalamic sleep factors
- In autism, abnormalities of serotonin synthesis, metabolism, and transport have been reported
- The serotonin transporter gene (*SLC6A4*) has been extensively studied in autism as well as in anxiety disorders and ADHD

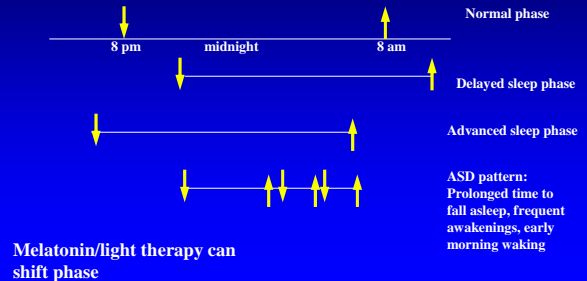
Sleep and Autism are Interrelated: Neurochemistry

- Sleep and autism share similar neurotransmitters
 - ✓ **Melatonin**
- Melatonin is a pineal hormone that regulates the sleep-wake cycle and promotes sleep
- Prolonged sleep latency and decreased sleep time in autism are consistent with a circadian rhythm disorder
- Deficiencies in melatonin secretion and excretion have been documented in autism (Nir, 1995; Kulman, 2000; Tordjman, 2005).

Melatonin



Sleep Phase



Other Causes of Insomnia in Autism

- Symptomatology related to disorder can influence sleep
 - ✓ Increased sensitivity to touch, sound, light
 - ✓ Need for structure, predictability
 - ✓ Anxiety
- Familial influences can affect sleep
 - ✓ Worn-out parents who don't have the energy to establish a bedtime routine
 - ✓ "Parental guilt" about teaching children how to fall asleep on their own
- Coexisting epilepsy, mental retardation, or psychotropic medications can also affect sleep

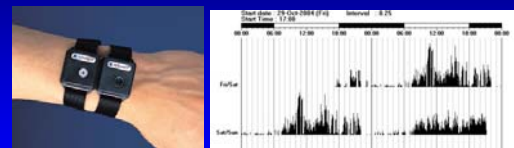
Evaluation of Insomnia: Key points

- Ask about bedtime, waketime, awakenings
- Is there a regular bedtime?
- Is there a bedtime routine?
- Are there any habits (caffeine, stimulating activities before bed) that can be interfering with sleep?
- Are there any medications or psychiatric comorbidities that can be interfering with sleep?
- Is there evidence of a primary sleep disorder (such as obstructive sleep apnea) contributing to insomnia?

Measuring sleep in autism: Actigraphy

- Polysomnography is gold standard for detecting obstructive sleep apnea, but may not be as useful for monitoring insomnia
- Sleep diaries and questionnaires are highly subjective
- Actigraphy has promise. measures movement as a surrogate for wakefulness. It is an objective, non-invasive, minimally cumbersome, and cost effective way to measure sleep over weeks, and measure response to treatment
- **Does** require parents to keep accurate sleep diaries as actigraph needs to be interpreted in context of when child went to bed and arose from bed

Actigraphy: movement quantifiers



How do we achieve this?



Insomnia- Behavioral Treatment

Bedtime resistance/difficulty falling asleep

- Bedtime routine: 20-30 minutes recommended
- Regular sleep time to help synchronize rhythms
- Avoidance of stimulating activities (computer, TV) 1 hour before bedtime
- Getting enough exercise during day
- Assess the sleeping environment: maybe door needs to be left open? A nightlight needs to be used?
- Teaching child to fall asleep on his/her own—options include “rocking chair technique” (courtesy of Dr. McGrew)

Visual Supports in bedtime routine



Weighted blankets



Insomnia- Behavioral Treatment

Night wakings

- Review bedtime habits: has child learned fall asleep on his/her own?
- Avoiding playing with the child when entering room or when returning child to bed “Back to Bed”
- Reward in morning for sleeping through the night
- Sticker book for sleeping through the night
- Bedtime pass (Friman et al, 1999)
- “Sleep Better” reference (Durand, 1998)

Insomnia- Pharmacological Treatment

- Best used after behavioral treatments have been tried unsuccessfully, and in combination with behavioral therapies
- Whenever possible, choose a medication that will treat a comorbidity such as epileptic seizures, anxiety, or a mood disorder
- Start at low doses, as children with developmental disabilities may be more susceptible to adverse effects and be less able to communicate them effectively

Insomnia- Pharmacological Treatment

- Epilepsy: Most antiepileptic medications are sedating, and maximizing nighttime dose can promote sleep.
- Bipolar disorder, irritability, aggression, self-injurious behavior: sedating atypical neuroleptics such as risperidone
- Anxiety or depression: sedating antidepressants
- Primary insomnia: melatonin, clonidine, diphenhydramine, benzodiazepines

Insomnia- Melatonin

- Melatonin has been used successfully to treat insomnia in ASD and a variety of other neurodevelopmental disorders in retrospective and prospective studies, although double-blind placebo studies have not been carried out to date.
- Appealing to parents --“dietary supplement” with few adverse effects
- Andersen et al, 2006 (retrospective): 113 children with ASD treated with 1-6 mg melatonin before bedtime. Parents reported improved sleep in 89%.
- Paavonen et al, 2003 (prospective): 15 children with Asperger disorder, treated with 3 mg melatonin 30 minutes before bedtime for 2 weeks, showed a 50% reduction in sleep latency, as measured by actigraphy.

Future Directions

- Define impact of insomnia in ASD more thoroughly, including impact of treating insomnia on daytime behavior and parental stress levels.
- Determine role of melatonin and other neurotransmitters in sleep and ASD. Is there a melatonin deficiency in ASD? In poor sleepers more than good sleepers?
- Carry out a pilot trial of melatonin for insomnia in ASD
- Carry out a behavioral intervention for insomnia in ASD
- Further characterize role of actigraphy in assessing sleep
- Integrate our work with genetics and circadian research

Summary

- Autism and sleep are interrelated
- Insomnia is the prominent sleep concern reported by parents of children with autism
- The causes of insomnia are likely multifactorial, and many causes are treatable
- Further research will be necessary to determine whether treatment of insomnia and other causes of sleep disturbance in autism positively influence daytime behaviors and reduce autism symptomatology

Collaborators

| | |
|-------------------------|--------------------------------|
| Wendy Stone, PhD | Karen Adkins, RN, CCRC |
| Susan McGrew, MD | Lydia MacDonald, BS |
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| Carl Johnson, PhD | Peter and Pagan Howard, RPSGTs |
| Jim Sutcliffe, PhD | Lily Wang, PhD |

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Any questions?



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