Myotonic Dystrophy and Sleep

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DM Research at Stanford

• Sleep and CNS evaluations in young myotonic dystrophy adults

• Coordinated clinical and animal studies of CNS in DM with University of Florida (Swanson, Ranum) and Stanford Sleep Center (Mignot, Nishino)

• Specimen Repository

• Investigation of DM changes in neuropsychology, MRI, Electrophysiology, CSF, blood biomarkers
Conclusions

• Myotonic Dystrophy (DM) affects many body systems that directly or indirectly alter sleep

  • Altered throat and breathing musculature can reduce sleep quality
  • Direct effects on brain sleep centers can alter sleep patterns and quality of sleep

• Abnormal sleep in DM affects behavior, cognition and quality of life

• Treatments may improve sleep quality in DM

• Research is shedding light on DM sleep including CNS causes and effects
Organization of Talk

• Global effects of DM and how they impact sleep
• Specifics of sleep abnormalities in DM
• Ongoing DM Sleep Research
• Questions (and Answers?)
First – Questions for the audience

• For individuals with DM (directly or family report)
  • How many, at some time, have been told to use breathing support at night (e.g., CPAP, BiPAP, AVAPS, Curiass)
  • How many actually ever tried it?
  • How many continue(d) to use it?

• How many have been prescribed a stimulant to combat daytime sleepiness (Provigil/Nuvigil/modafinil; Ritalin/dexedrine; Cylert/pemoline)?
  • How many have ever tried it?
  • How many continue to use it?
DM Alteration of Sleep

Affected DM Systems That Alter Sleep

Proximal Cause

DM Genetic Change

Skeletal Muscle
Brain
Heart
Endocrine
Gut

Breathing Strength
Airway Obstruction
Sleep Quality
Sleep Length
Sleep Cycle
Muscle Fatigue
Mental Fatigue
Metabolic

DM Dysfunctions That Affect Sleep & Stamina
DM muscle pathology
- muscular dystrophy
- congenital myopathy
- metabolic myopathy
- myotonia
RNA Changes Precede Pathology

Muscle Bx @ 28y/o

Muscle Bx @ 36y/o

Savkur, et. al. AJHG, 74:1309; 2004
How is ClC-1 altered in DM?

Alternate Splicing

Charlet-B, et. al., Mol Cell, 10:45, 2002

ClC-1 Immunofluorescence

Mankodi, et. al., Mol Cell, 10:35; 2002
DM muscle pathology
- congenital myopathy
- muscular dystrophy
- metabolic myopathy
- myotonia
DM Muscle Involvement Directly Affecting Sleep
DM Alteration of Sleep

Affected DM Systems That Alter Sleep

Proximal Cause

DM Genetic Change

Skeletal Muscle
Brain
Heart
Endocrine
Gut

DM Dysfunctions That Affect Sleep & Stamina

Breathing Strength
Airway Obstruction
Sleep Quality
Sleep Length
Sleep Cycle
Muscle Fatigue
Mental Fatigue
Metabolic
What do DM patients experience regarding sleep?

• Greater than normal need for sleep
• Inability to awaken quickly
• Snoring, dry eyes, dry mouth during sleep
• Fragmented sleep patterns
• Excess or abnormal sleep movements
• Sleep paralysis or sleep-related hallucinations or excessively vivid dreams
• Self-medication or prescriptions to wake-up or fall asleep
Conclusions

• Myotonic Dystrophy (DM) affects many body systems that directly or indirectly alter sleep
  • Altered throat and breathing musculature can reduce sleep quality
  • Direct effects on brain sleep centers can alter sleep patterns and quality of sleep
• Abnormal sleep in DM affects behavior, cognition, quality of life, and overall health (heart, energy, etc.)
• To treat sleep abnormalities in DM
  • Provide excellent comprehensive baseline care
  • Thoroughly evaluate and determine cause of sleep disorder