

Narcolepsy: A Sleeping Disorder



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Presentation Outline

- History and Background Information on Narcolepsy (Debbie)
- Narcolepsy Effects on Sleep (Peter)
- Canine Model of Narcolepsy (Aziz)
- Neural Correlates of Narcolepsy (Ken)
- Questions (Everyone)

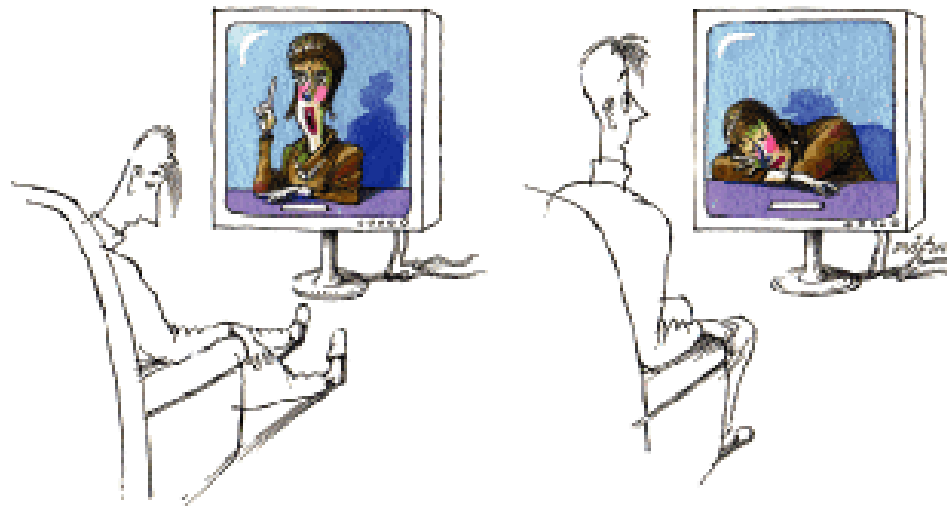
History of Narcolepsy

- In 1880, Jean Bapiste Gelineau first described Narcolepsy as
- “a rare neurosis...characterized by an urgent necessity to sleep, sudden and of short duration which recurred at intervals more or less long”
- William Dement and his colony of narcoleptic dogs

Definition

Narcolepsy (n.): A disorder due to a malfunction of the sleep/wake cycle regulating system in the brain, caused by the lack of an important chemical in the part of the brain responsible for controlling sleep

WHAT IS NARCOLEPSY?



THIS ISN'T....

THIS IS!

Narcolepsy in the Movies



From "Deuce Bigalow, Male Gigolo" (1999)

Characteristics of Narcolepsy

- Daytime sleepiness
- Cataplexy
- Sleep Paralysis
- Instantaneous REM sleep
- Hypnagogic Hallucinations

1 in 2000 (or 250,000) Americans have Narcolepsy



**While less than 50,000 are aware of their
own disease!**

Normal Sleep/Wake Cycle

- Sleep is not merely passive
- Normal sleep occurs with a distinct cycle of stages:
 1. Waking state
 2. 4 stages of non-REM (Slow Wave)
 3. REM sleep

REM Sleep

- Rapid Eye Movements
- Neocortex activation similar to the waking state
- Makes up 20% of sleep duration
- Occurs **70-90 minutes** into sleep
- Muscular paralysis

Narcoleptic Sleep Cycles

- Onset of sleep = less than 10 minutes
- Poor nocturnal sleep contributes to feelings of sleepiness in the morning
- REM sleep = less than 20 minutes
- Quick onset of REM sleep causes inadequate rest, other mental problems
- Hallucinations and nightmares

REM Sleep and Narcolepsy

- Loss of muscle control resembles a neurological protective of REM sleep
- Hypnagogic hallucinations, illusions similar to dreams
- Sleep paralysis where after falling to or waking from sleep, a person finds that they cannot move

Canine-Human Correlation

- Canines and Humans share similar phenotypical, and physiological characteristics for narcolepsy.
- 2 Hypotheses for Human Narcolepsy
 - 1. Disease occurs at immediate onset
 - 2. Disease occurs at a delayed onset

Canine Model for Narcolepsy

- Found Axonal Degeneration in:
 - Amygdala
 - Basal Forebrain
 - Entopenuncular Nucleus
 - Medial Septal Region

Canine Model

- Found that Narcolepsy was caused by a mutation in:
 - Orexin Peptide Gene
 - Involved with sleep and wake cycles
 - Hypocretin Receptor 2 Gene (Hctr2)
 - Involved with excitatory system

Hypocretins and Narcoleptics

- 85-90% of Narcoleptics possess a reduction in Hypocretin Neurons

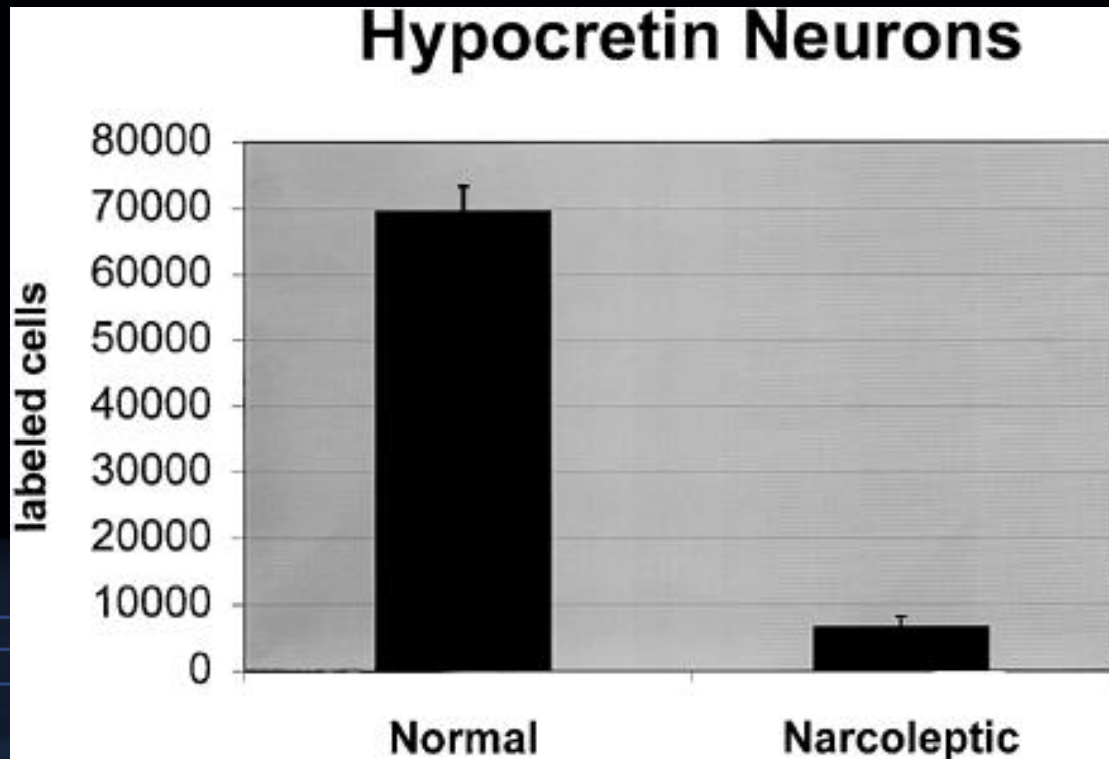


Figure 1. Number of Hcrt Cells Decreased in Narcoleptics

Role of Hypocretins

- Modulate neurons involved with REM sleep
- Help the interaction between the aminergic and cholinergic systems
- May produce wakefulness and depress REM sleep
 - Stimulation of hypocretin receptor 2 gene

Neurological Correlates

- Dorsolateral Pons and Medial Medulla
 - Normal: suppresses muscle tone during REM
 - Narcoleptics: causes cataplexy
- Amygdala
 - Normal: aids perception of emotional responses
 - Narcoleptics: activates of Brain stem's motor inhibitory system causing cataplexy through strong emotional triggers
- Hypothalamus
 - Normal: regulates the excitatory system
 - Narcoleptic: possesses a reduction Hypocretins and thus causes a decrease in Hcrt activation, which results in sleepiness

Narcoleptic Cures

- There is no cure for narcolepsy
- However, some drugs help with the many of the symptoms
 - **Amphetamines**- help with day time sleepiness
 - **Antidepressants**-help with suppressing REM, cataplexy, paralysis, and hallucination
 - **Hypocretin**- helped cure dogs of cataplexy

Narcolepsy and Consciousness

- One theory proposes that “the lack of brainstem activation may be related to the preservation of consciousness of the outside world that occurs during cataplectic states but not during REM sleep periods”

Questions

- What's a Narcoleptic's Favorite band?
 - REM

References

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