

Retrospective Analysis of Metabolic and Medicinal Effects in Pediatric Narcolepsy Data

Introduction

Narcolepsy

- Hormonal Imbalance
- Orexin/Hypocretin—wakefulness and appetite
- Lack of Orexin in the brain due to destruction of the cells—produce cataplexy
- Affects 1 in 2000 individuals (Nishino et al., 2005)
- 75% - Onset before the age of 12 (Wu, 2013)
- Young field of study
- 83.3% of patients showed cataplexy (Wu, 2013)

Diagnosis

- MSLT— Multiple Sleep Latency Test
- 5 chances to nap
- <8 min: Chronically Sleep Deprived
- 20 minutes total
- Sleep conducive conditions
- Sleep Study (PSG: Polysomnography)



<http://www3.hdmx.com/photos/11/64/12/2572958/7/628e471.jpg>

Purpose

- Seldom researched
- No research relating growth to narcolepsy
- Could open the doors to waves or research
- Revolutionize pediatric narcolepsy treatment
- Dietician or Pediatrician may need to be present

Research Questions

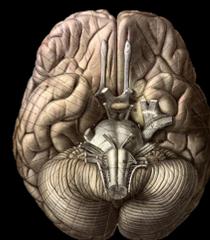
- RQ₁: Do adolescent patients with narcolepsy grow at a normal progression?
- RQ₂: Do treatments designed to regulate sleep and/or mitigate the effects of narcolepsy such as Xyrem and/or Nuvigil help in restoring previously impaired growth and/or weight gain and loss?
- RQ₃: Do pediatric patients with Narcolepsy show signs of being overweight?

Hypotheses

- H₁: If Narcolepsy in children is related to growth, then children affected by Narcolepsy will show clear signs of stunted growth when compared to other children in their age group.
- H₂: Pediatric Narcolepsy patients will show signs of rapidly gaining weight after onset occurs.
- H₃: Children will show signs of restored growth when under the treatment of Xyrem and/or Nuvigil.
- H₀: If children are diagnosed with Narcolepsy, then no physiological nor growth effect will be observed.

Nomenclature History

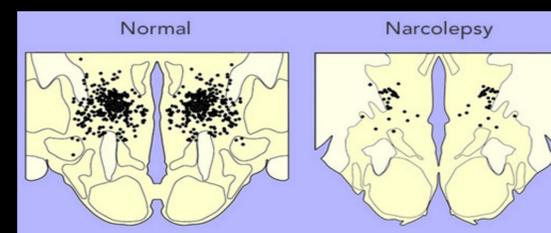
- Two experiments (1998)
- University of Texas Southwestern Medical Center at Dallas
- Orexin – appetite stimulating (Orexigenic) (Yanagisawa, 1998)
- Hypocretin – Interaction with hypothalamus (Kilduff, 1998)



http://upload.wikimedia.org/wikipedia/commons/7/7a/foho_1009_021.png

Orexin/Hypocretin

- Neuropeptide—chemical signals secreted by the endocrine system (Lateral Hypothalamus)
 - Diagnosis Marker (Mignot, 2007)
 - Controls wakefulness (Sinton, 2010)
- Regulates nocturnal sleep arousals and desire to eat



<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1378918/>

Methods

Participants

- 9 ≤ Age ≤ 20
- n=16; 4 Male, 12 Female in statistics portion
- μ_{age} = 17.31 Years
- n=4; 1 Male, 3 Female in growth chart portion
- μ_{age} = 15.5 Years

Confidentiality

- Patient Consent Letters administered
- Included Background on research
- Confidentiality for growth charts stricter

Epworth Sleepiness Scale

- Two copies attached in patient consent envelopes
- Patients asked to return both copies
 - Prior
 - After
- Universal sleep scale used to determine the degree of severity of various sleeping disorder (i.e.: Narcolepsy)

Analysis

- Comparing given growth information to CDC's official growth charts for adolescents
- General trends and Common patterns
- Qualitative v Quantitative

Review of Literature

PTSD

- Poor sleep quality
- Frequency of disturbances similar to narcolepsy (Liempt et al., 2011)
- Human Growth Hormone
- PTSD (Liempt et al., 2011)
- Interrupted Sleep by Awakenings
- Significantly Lower GH Levels
- Adult

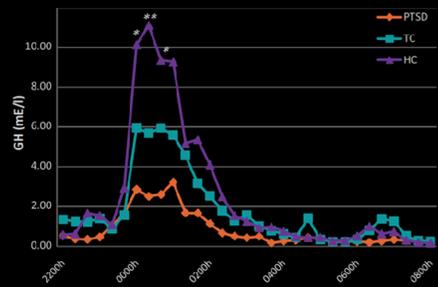


Table 2 Growth hormone secretion, sleep and memory in PTSD and controls.

	PTSD (n = 8)	TC (n = 14)	HC (n = 12)	Group comparison
Growth hormone secretion				
AUCI M (SD)	19.1 (12.9)	37.1 (22.3)	58.6 (24.2)	p = 0.01*
AUCg M (SD)	25.6 (12.8)	55.0 (43.7)	76.0 (44.8)	p = 0.02*
Polysomnography				
PTSD (n = 12)		TC (n = 15)	HC (n = 15)	Group comparison
Awakenings (11 pm to 3 am) M (SD)	8.5 (3.8)	4.3 (2.8)	5.1 (2.2)	p = 0.01*
% SWS M (SD)	20.1 (5.9)	20.0 (5.6)	25.3 (12.6)	p = 0.63
Total sleep time M (SD)	405.4 (43.6)	420.8 (36.7)	417.0 (44.5)	p = 0.532
Minutes of SWS M (SD)	77.0 (29.8)	83.5 (25.17)	92.6 (26.0)	p = 0.48

Obstructive Sleep Apnea

- Height, Weight, GH
- OSA (Zhang et al., 2015)
- Infants
- Frequent Micro Disturbances
- Significantly Lower GH Levels

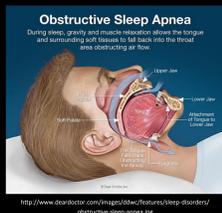


Table III. Height, weight, IGF-1, and z-score of control and patient group

	Height, cm		Weight, kg	
	Control	OSAS	Control	OSAS
Before T&A	122.2 ± 15.85	111.2 ± 13.47	24.06 ± 7.48	17.88 ± 4.71
3 months	124.0 ± 15.76	114.9 ± 13.22	24.86 ± 7.43	19.26 ± 4.75
6 months	126.1 ± 15.71	117.9 ± 13.02	25.48 ± 7.39	20.50 ± 4.51
1 year	129.2 ± 15.90	122.9 ± 12.88	26.56 ± 7.22	22.28 ± 4.70

Implications:

PTSD

- Growth hormone secretion deficiency is strongly associated be related to sleep fragmentation

OSAS

At every time period:

- Weight and heights were less in the OSAS (Obstructive Sleep Apnea Syndrome) category
- OSAS stunts growth and development
- Growth recovery is possible

Results



- Symbols not shown in a solid continuous line are data points
- Yellow lines represent the premature stabilization of heights in the two patients of age
- Red line represent where the natural stabilization of heights should occur

Figure 1.1

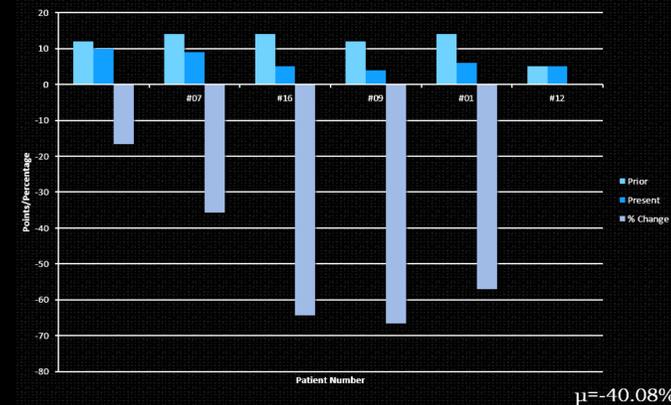
Situation	Would never doze	Slight chance of dozing	Moderate chance of dozing	High chance of dozing	My score
Sitting and reading	0	1	2	3	
Watching TV	0	1	2	3	
Sitting inactive in a public place	0	1	2	3	
Lying down to rest in the afternoon	0	1	2	3	
Sitting and Talking to a friend	0	1	2	3	
Sitting quietly after lunch	0	1	2	3	
In a car, with your parents, stopped at a traffic light	0	1	2	3	
As a passenger on a long drive in the car	0	1	2	3	

- Sample of the modified Epworth Sleepiness Scale (ESS) distributed during study
- Average change was calculated to measure effectiveness on quality of life



- Symbols not shown in a solid continuous line are data points
- Lower red line represents normal weight projection until onset of narcolepsy
- Upper red line represents skewed weight projection after the onset of narcolepsy

Figure 3.1



- ESS scores represented by positively valued boxes
- Percent change represented by the negatively valued boxes

Discussion

- Pediatric narcolepsy - strongly correlated with impaired growth and uncontrollable weight changes, especially in females
- Sample size too small to render significant or ensure validity
- H₁ supported
- Study pioneers research in the field of pediatric narcolepsy
- Weight did not rapidly increase *consistently*
- H₂ *partially* not supported
- Medicine used, Xyrem and/or Nuvigil, was shown to improve the quality of life of the patient
- H₃ *partially* supported
- Quality of life improvement shown via Epworth Sleepiness Scale
- Research should be repeated to ensure validity and further explore this field

Future Research

- Larger sample size
- More diverse demographics
- National
- Using night time intravenous growth hormone secretion tests

Limitation

- Small sample size (n=4)
- Possible non-response and response bias
- Lack of research to compare results
- Further research is needed.

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