17th Annual Sleep Medicine Virtual Course

Saturday, March 22, 2025

Evaluation Hypersomnia

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Conflict of Interest Disclosures for Speakers

Clete A. Kushida, MD, PhD, FAASM

disclosed relationships with Alkermes, Inc. (consultant), Asleep (consultant), Avadel Pharmaceuticals (USA), Inc. (Scientific Advisory Board), Cerebra Health Pharmaceuticals Inc. (Scientific Advisory Board), NLS Pharmaceutics AG (consultant)

The relevant financial relationships have been mitigated.

OVERVIEW

- Characteristics
- Assessment, Evaluation, and Diagnosis

EPIDEMIOLOGY

Estimated to occur in 0.02 - 0.18% of the general population, affecting about 200,000 Americans

Finland	0.025%
France	0.045%
Israel	0.0002%
Japan	0.16%
United Kingdom	0.04%

CHARACTERISTICS OF PATIENTS WITH NARCOLEPSY

VARIABLE	PATIENTS WITH NARCOLEPSY (n = 59)
MWT sleep latency, min, mean (SD)	8.7 (6.2)
ESS	17.2 (2.8)
Baseline CGI-S, n (%)	
Moderately ill	17 (28.8)
Markedly ill	21 (35.6)
Severely ill	12 (20.3)
Extremely ill	8 (13.6)
FOSQ-10 total, mean (SD)	11.4 (2.9)
SF-36v2	
Physical Component Summary, mean (SD)	46.1 (9.8)
Mental Component Summary, mean (SD)	44.8 (9.5)
WPAI:SHP (employed patients)	
% Work time missed, mean (SD)	14.9 (26.0)
% Impairment while working, mean (SD)	48.4 (23.9)
% Overall work impairment, mean (SD)	61.5 (22.5)
% Activity impairment, mean (SD)	65.8 (21.5)
EQ-VAS total score, mean (SD)	69.4 (20.3)

98.3%

CGI-S = Clinical Global Impressions Scale; EQ-VAS = EuroQol Visual Analogue Scale; FOSQ = Functional Outcomes of Sleep Questionnaire; WPAI:SHP = Work Activity and Impairment Questionnaire: Specific Health Problem

Emsellem HA, et al. *Sleep Med*. 2020;67:128-136.

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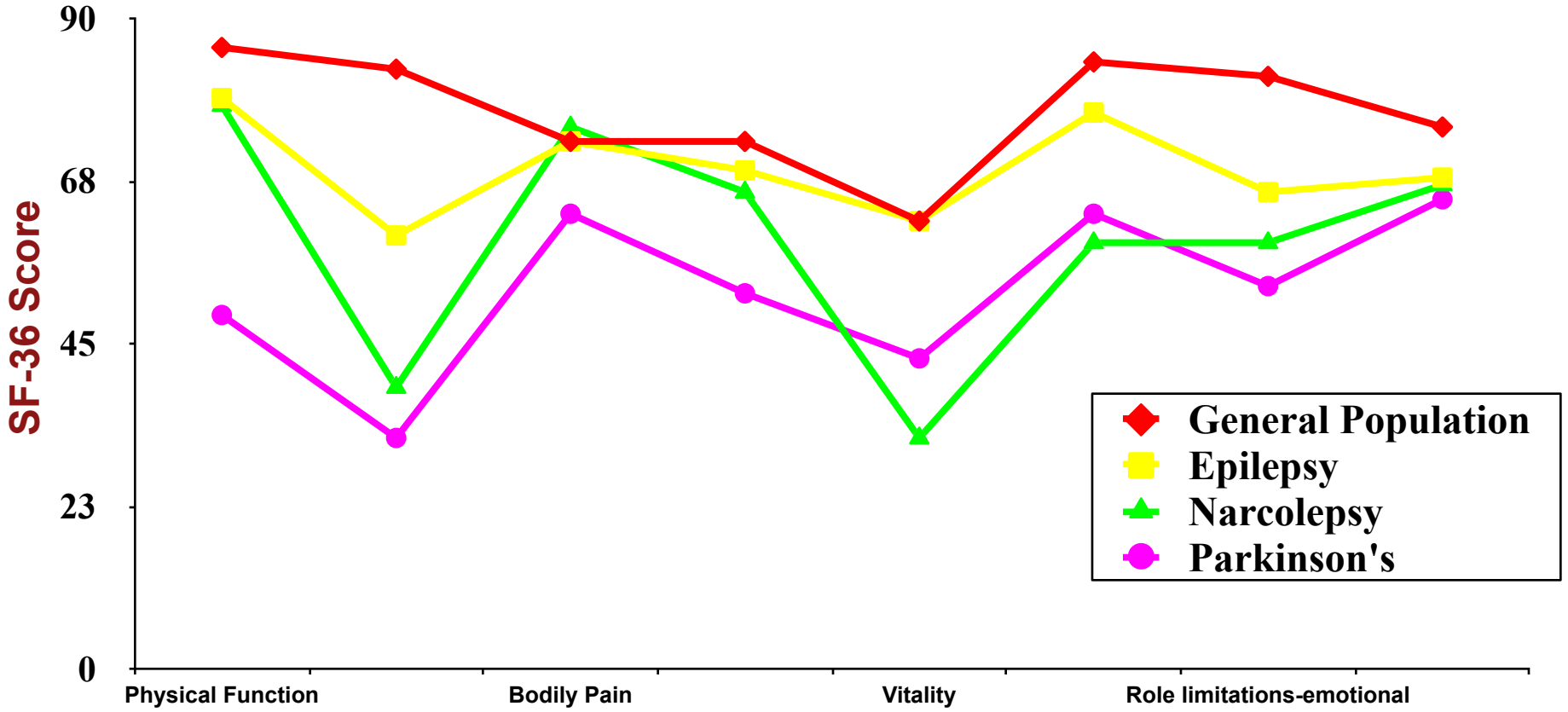
QUALITY OF LIFE

Narcoleptic patients report significant role limitations due to physical problems, lowered vitality, lower social functioning and role limitations due to emotional problems by the SF-36. Patients with narcolepsy are more impaired than patients with epilepsy, and almost as impaired as patients with Parkinson's Disease.



Sleep Academic Award Program, NHLBI and AASM; Adapted from Beusterien KM, Rogers AE, Walsleben JA, Emsellem HA, Reblando JA, Wang L, Goswami M, Steiinwald B. Health-related quality of life effects of modafinil for treatment of narcolepsy. SLEEP 1999; 22:757-765

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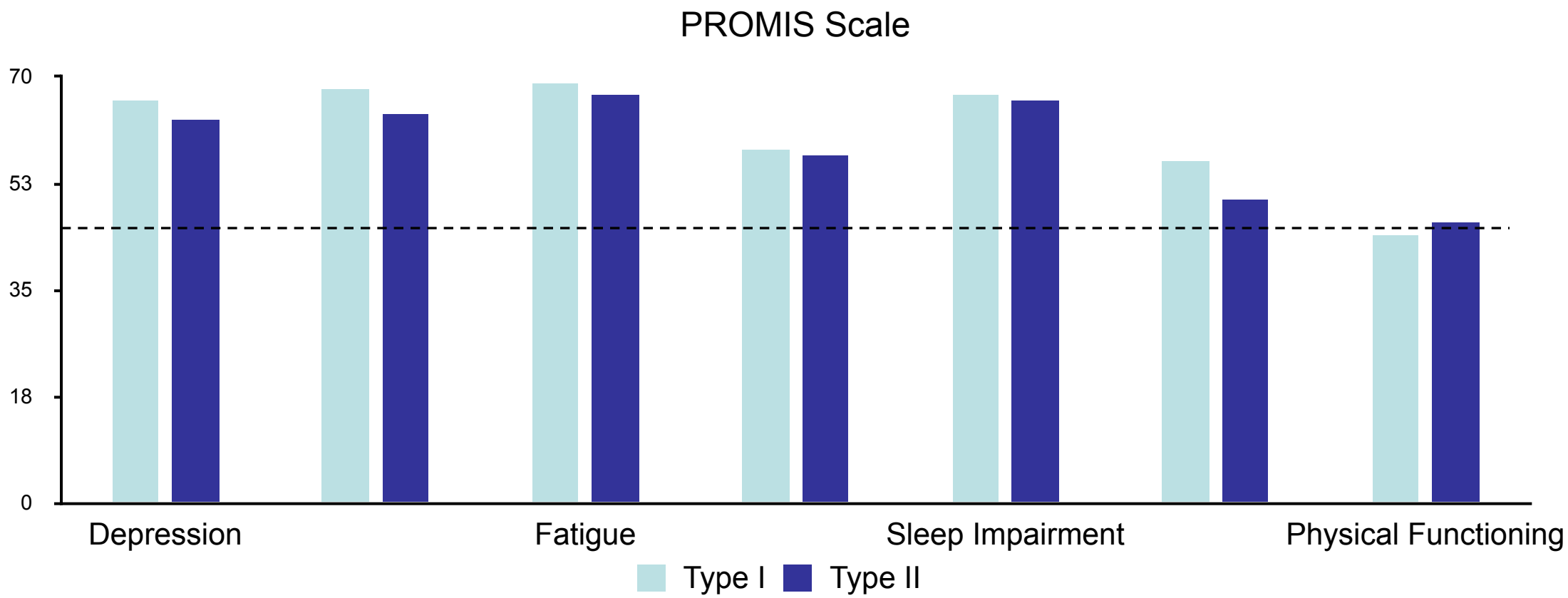
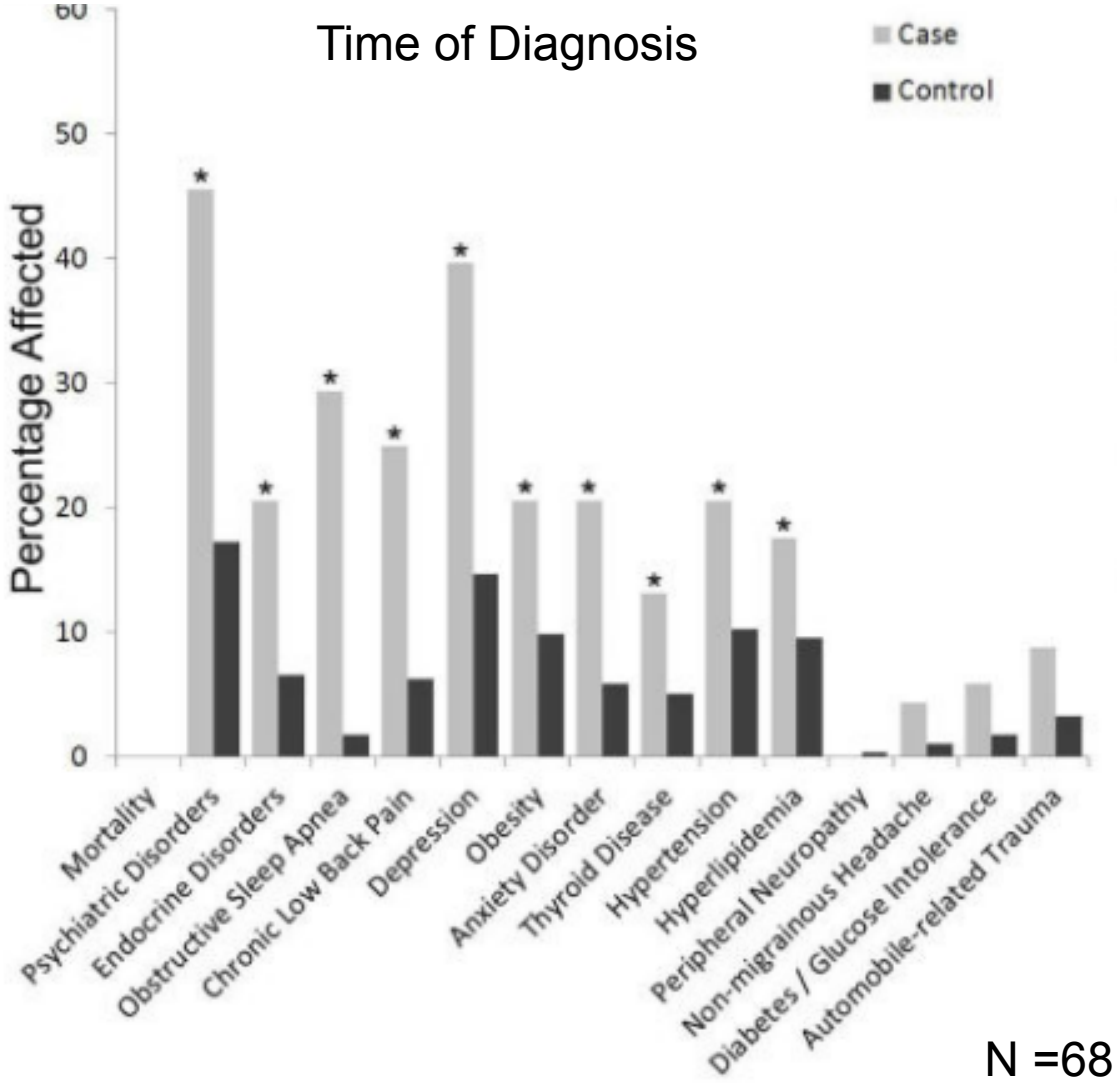
HEALTH-RELATED CHALLENGES

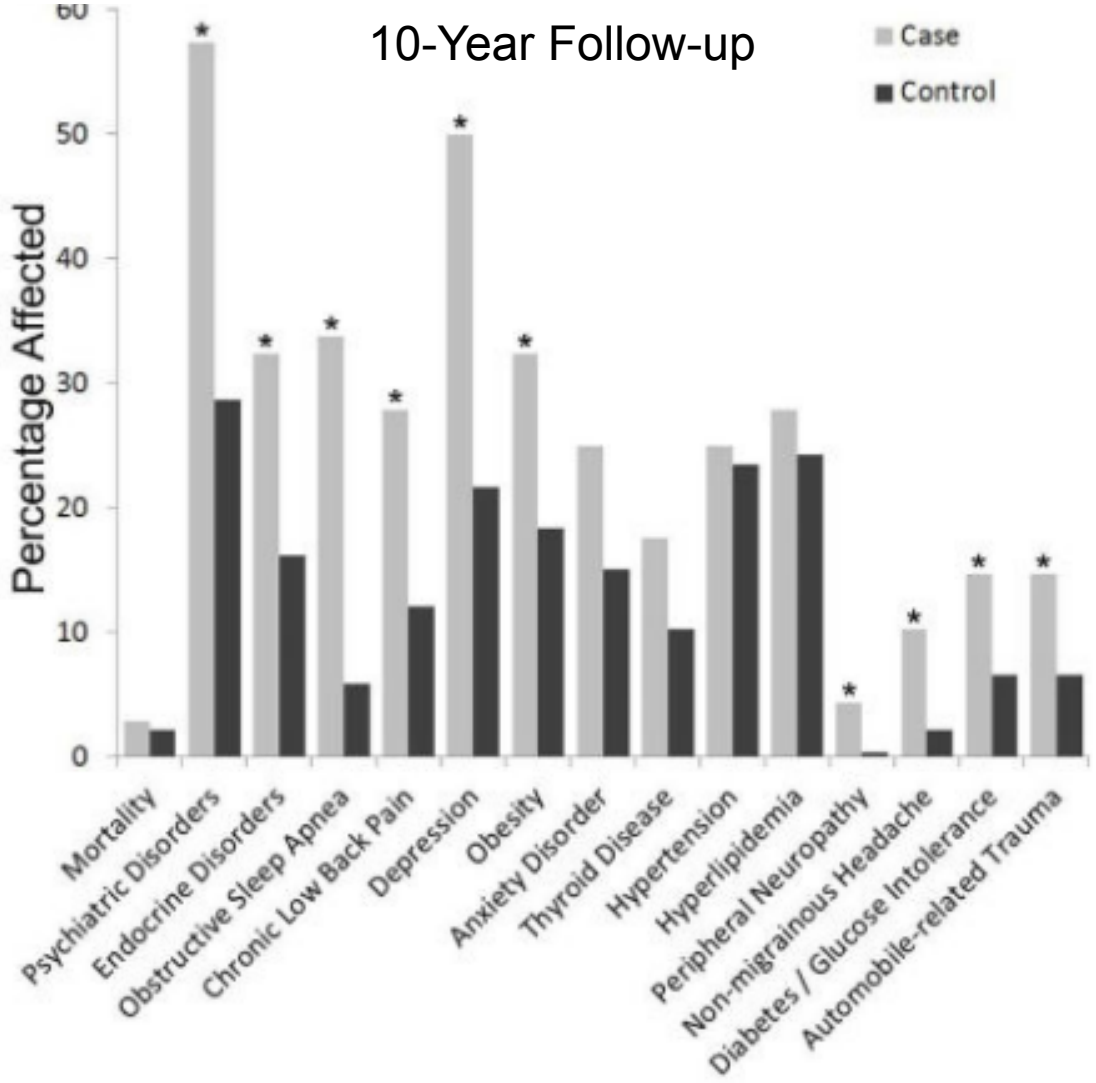


PROMIS = Patient-Reported Outcomes Measurement Information System

Ong JC, et al. *Behav Sleep Med*. 2021;19(2):145-158.

NARCOLEPSY COMORBIDITIES





N =68

Cohen A, Mandrekar J, St Louis EK, Silber MH, Kotagal S. Comorbidities in a community sample of narcolepsy. Sleep Med. 2018 Mar;43:14-18

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CARDIOVASCULAR BURDEN IN NARCOLEPSY

- BOND and CV-BOND revealed an increased risk of cardiovascular comorbidities and new-onset events in patients with narcolepsy, respectively, when compared to a non-narcolepsy cohort.
- CV-BOND further showed that there was an increase in CVD specifically, in addition to other claims database studies, which utilize insurance claim databases, may seek to provide understanding of the most commonly increased conditions in a specific cohort

CV-BOND: Increased Risk (expressed as OR) in Narcolepsy vs. Controls[1]

- Any stroke (1.71)
- Heart failure (1.35)
- Ischemic stroke (1.67)
- Major adverse cardiac event (1.45)
- Grouped instances of stroke, atrial fibrillation, or edema (1.48)
- Cardiovascular disease (1.30)

CV-BOND Study Limitations[2,3]

- Analysis did not control for autonomic dysfunction, concomitant medications, genetics risk factors, metabolic syndrome, or smoking
- Narcolepsy medication data not available to understand potential effects
- Controls were not body mass index (BMI)-matched to patients
- Large inclusion of NT2 patients compared to NT1
- Patient selection bias inherent in insurance claims database studies

(1) Ben-Joseph RH et al. *Sleep*. 2023;zsad161. (2) Black J et al. *Sleep Med.* 2017;33:13-18. (3) Barateau, L and Dauvilliers, Y. Sleep. Sleep, Volume 46, Issue 10, October 2023.

NARCOLEPSY AND HEALTHCARE RESOURCE UTILIZATION

DATA	HEALTHCARE RESOURCE
46%	Psychobehavioral Therapy
61%	Employees with an average of 51 sick leave days
28%	Received antibiotics
1 in 3	Hospitalized for any cause

- Those with narcolepsy commonly experience occupational problems, including impaired performance, decreased earning capacity, and increased rate of job loss due to termination.
- Misdiagnosis and delayed diagnosis may contribute to the socioeconomic burden of narcolepsy due to postponement of treatment and increased disease burden.

Kallweit U, et al. *J Clin Sleep Med.* 2022;18(6):1531-1537. Broughton R, et al. *Canad J Neurol*. 1981;8:299-304. Emsellem HA, et al. *Sleep Med*. 2020;67:128-136. Black J, et al. *Sleep Med*. 2014;15:522-529. Thorpy MJ, et al. *Am Health Drug Benefits*. 2017;10:233-241.

SURVEY OF NARCOLEPSY PATIENTS, TREATING PHYSICIANS, AND THE PUBLIC

- Narcolepsy is life-changing for 86% of those surveyed living with the disorder; however, 78% of the general public surveyed agreed they have no idea what it must be like to live with narcolepsy.
- 68% agreed they never feel like a normal person because of the disorder and 80% said living with narcolepsy is a daily struggle.
- 54% agreed narcolepsy controls their lives.
- 76% said the narcolepsy has affected important moments in their lives.
- 37% reported having failed a class at school or withdrew entirely because of narcolepsy.
- 25% said they have been fired from a job or demoted because of issues related to narcolepsy. For those who are currently employed, 66% reported that they feel worried about losing their jobs because of narcolepsy.

The Know Narcolepsy survey results (conducted by Versta Research among a total of 1,654 respondents on behalf of Harmony Biosciences LLC, in collaboration with Narcolepsy Network): https://narcolepsynetwork.org/surveyresults/

OVERALL IMPACT OF NARCOLEPSY ON QUALITY OF LIFE

STRAIN ON RELATIONSHIPS

EXCESSIVE DAYTIME SLEEPINESS

WORK PROBLEMS

CRITICAL THINKING IMPAIRMENT

BRAIN FOG

WORSENED HEALTH-RELATED QUALITY OF LIFE

INCREASED MVA RISK

MEMORY DIFFICULTIES

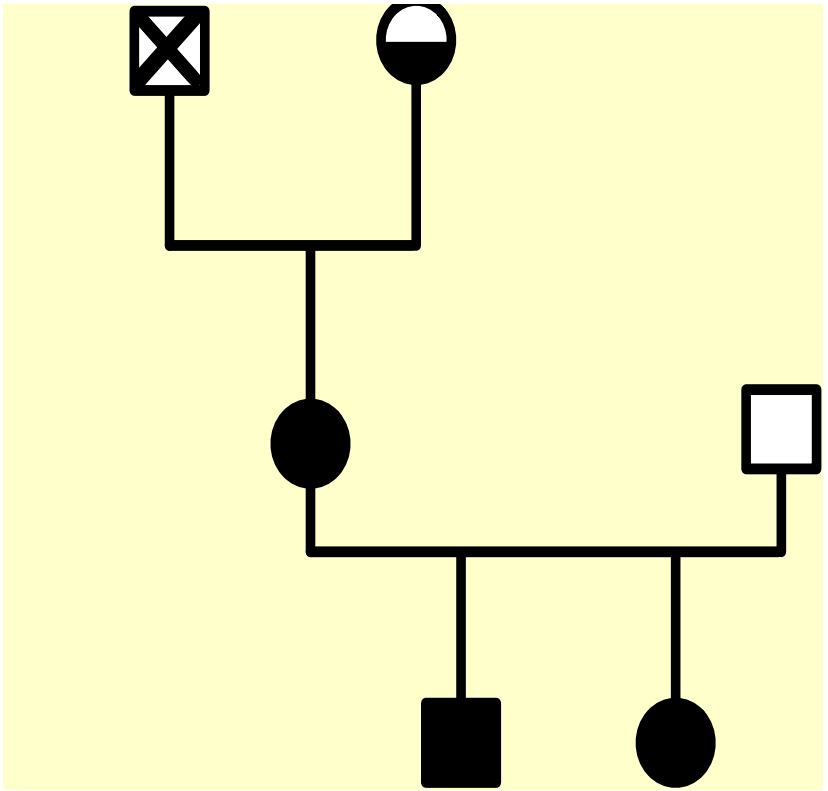
HRQoL = health-related quality of life

Emsellem HA, et al. *Sleep Med*. 2020;67:128-136. Bellebaum C, et al. Memory and cognition in narcolepsy. In: *Narcolepsy.* 2016. pp. 233-243. McCall CA, et al. *Ther Clin Risk Manag*. 2020;16:1099-1108.

NARCOLEPSY WITH CATAPLEXY

- Characterized by excessive daytime sleepiness, cataplexy, hypnagogic hallucinations, sleep paralysis, and fragmented sleep
- Commonly occurs in the second decade near puberty, but can occur at 3-6 years (rare below 5 years) and at 35-45 years
- Slight preponderance in males
- Familial aggregation

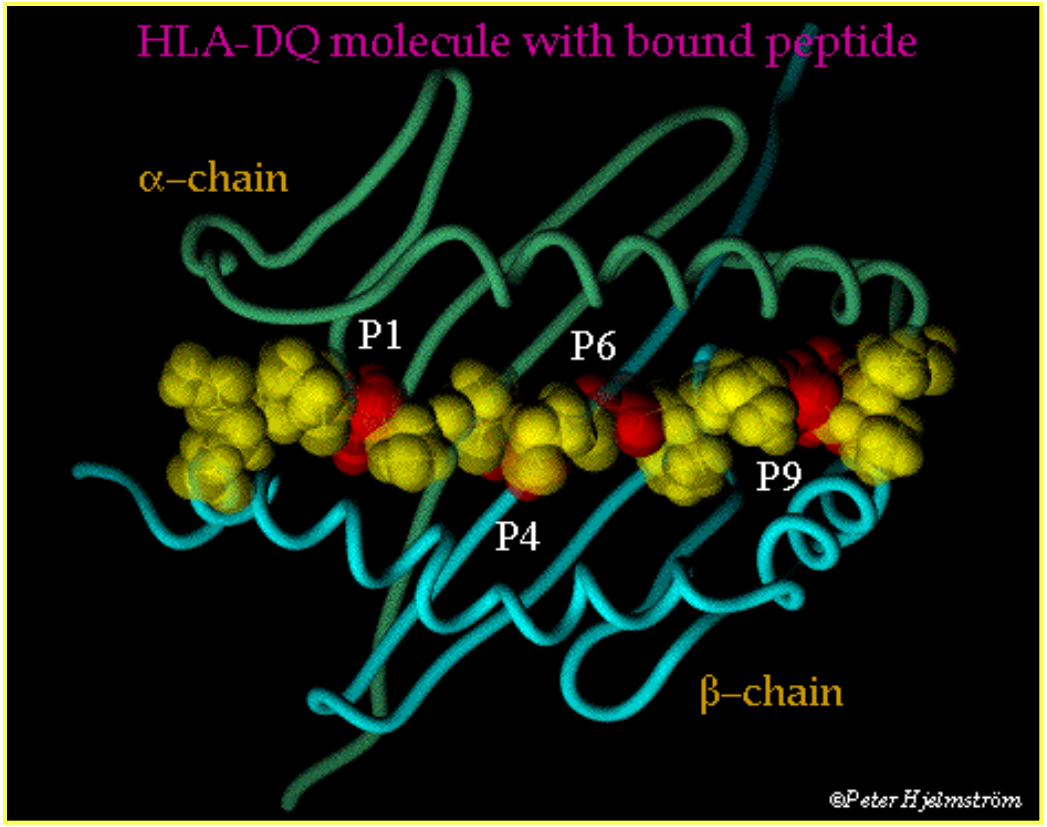
FAMILIAL ASPECTS



Sleep Academic Award Program, NHLBI and AASM-
Adapted from Mignot E. *Neurology* 1998;50(Suppl 1)

- Most cases of narcolepsy are sporadic
- 1-2% of first-degree relatives have narcolepsy-cataplexy (relative risk = 20-40)
- 4-6% of first-degree relatives may have isolated symptoms of narcolepsy

HUMAN LEUKOCYTE ANTIGEN



A 3-dimensional model of an HLA molecule with a bound peptide

- HLA-DR2 or DQB1*0602 is not sufficient to cause narcolepsy
- Additional gene(s) may be required
- Environmental factors play a role
- In some families, a non-HLA gene may confer narcoleptic susceptibility

Sleep Academic Award Program, NHLBI
and ©Peter Hjelmström © 1996

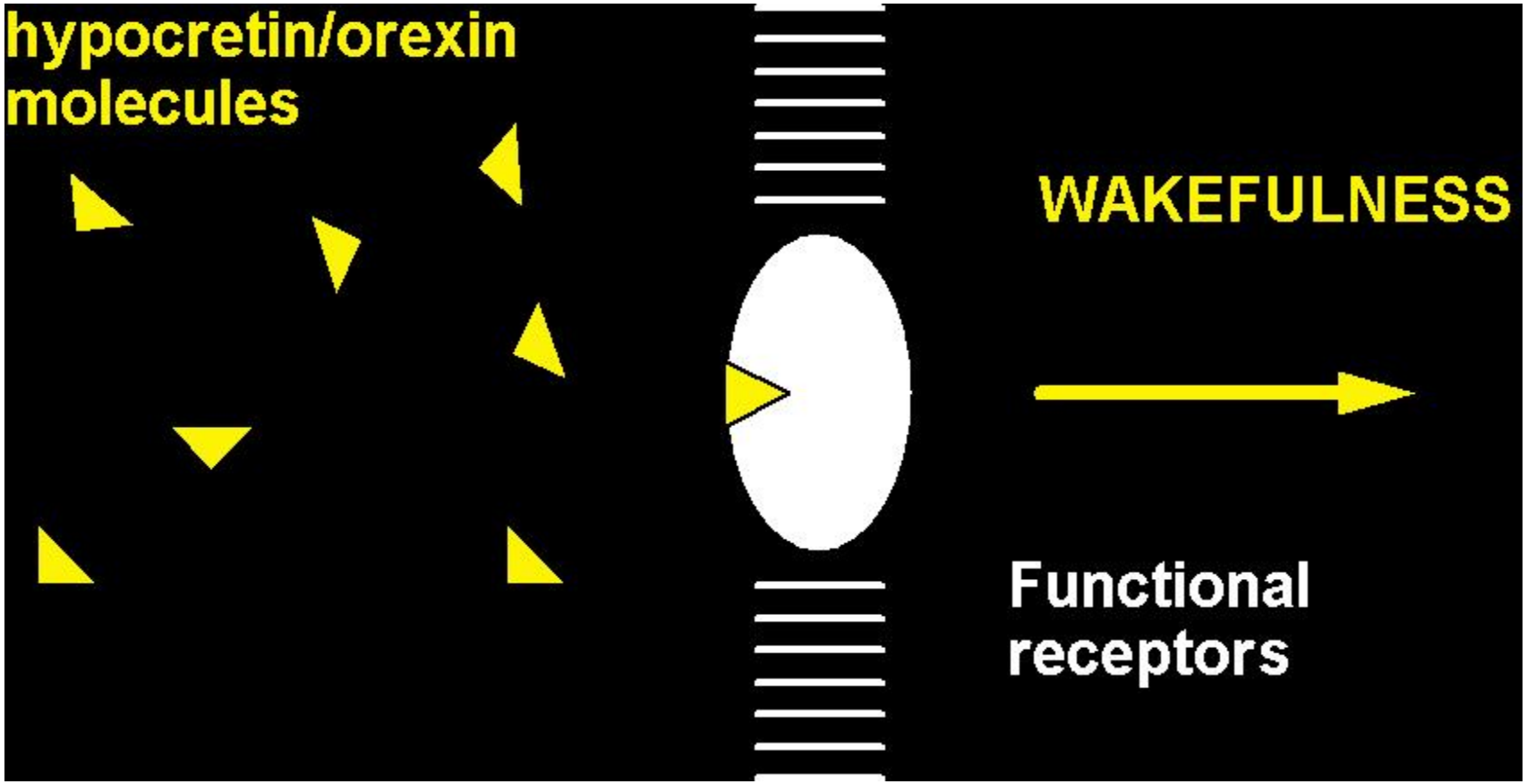
HLA ASSOCIATIONS

- HLA DQB1*0602 and HLA DRB1*1501 are associated with Caucasian and Asian narcoleptics; HLA DQB1*0602 is more specifically associated with African American narcoleptics
- HLA DQB1*0602 is the most common HLA marker associated with narcolepsy (90 - 93%)

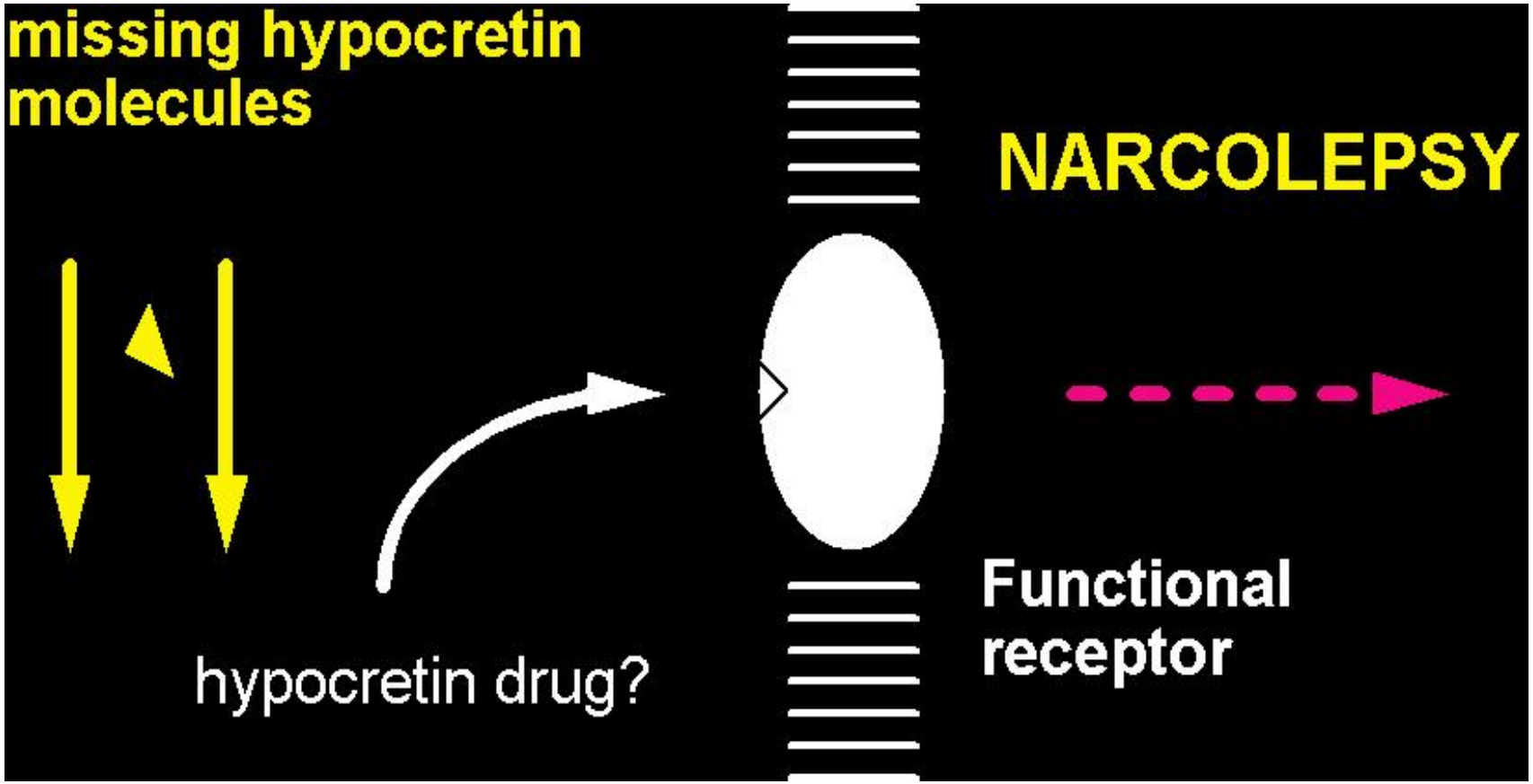
HYPOCRETIN-1 / OREXIN-A

- The majority of cases of narcolepsy with cataplexy are associated with a loss of up to 100,000 hypocretin-containing hypothalamic neurons
- Approximately 90% of narcoleptics with cataplexy (almost all with HLA DQB1*0602) have significantly decreased CSF hypocretin-1 levels

NORMAL OREXIN RECEPTORS

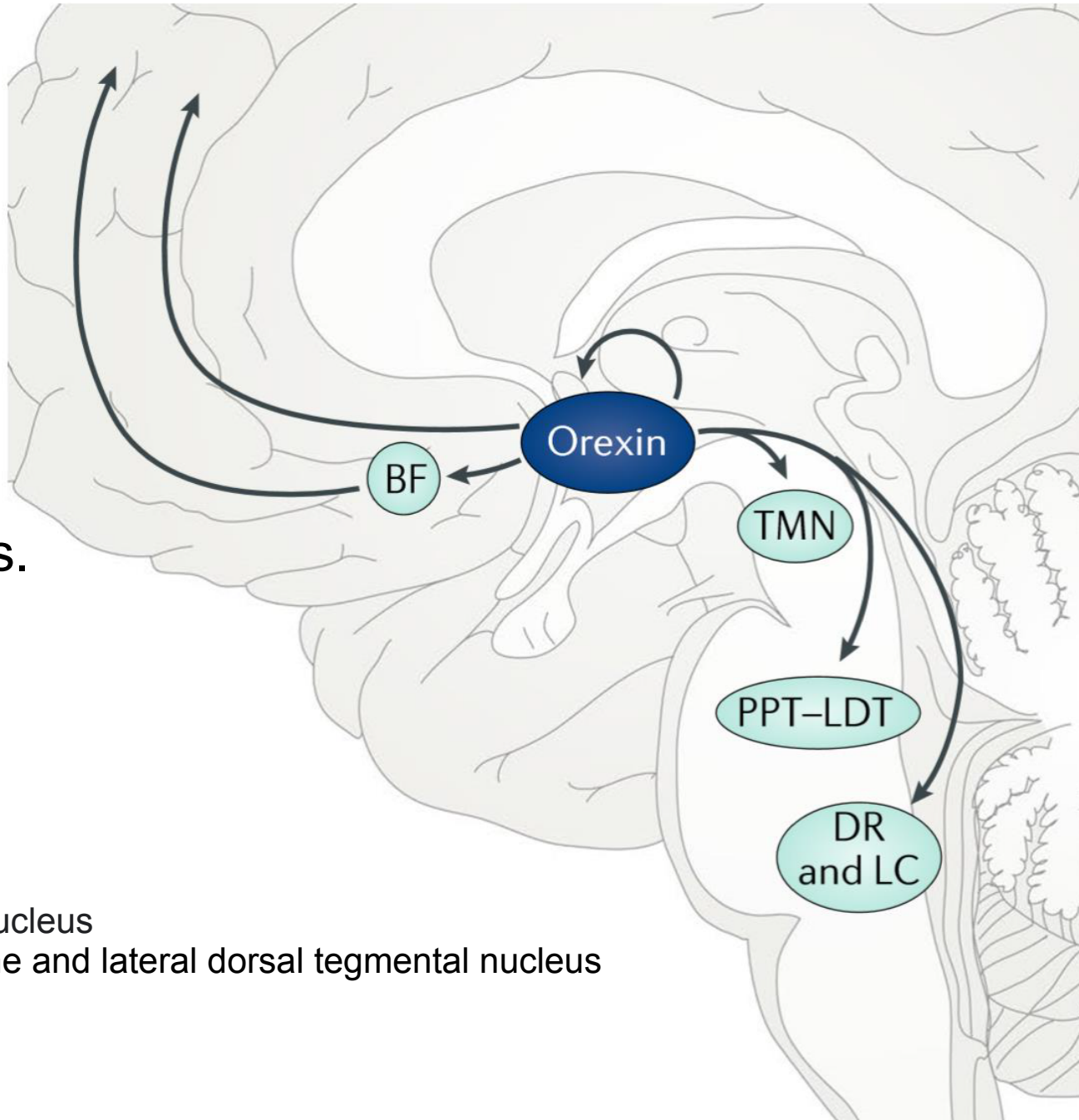


OREXIN DEFICIENCY



OREXIN PATHWAYS

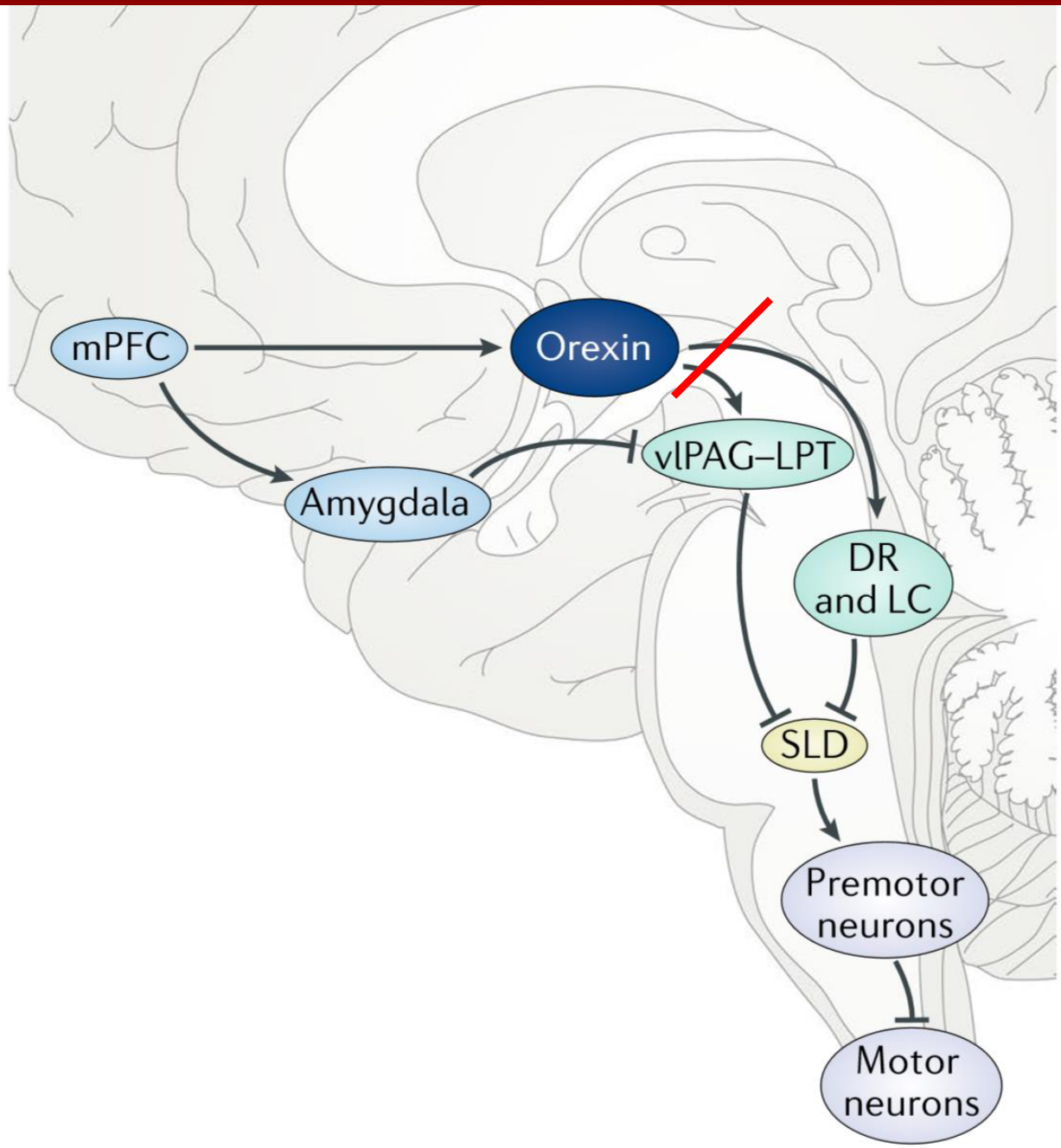
- Orexin neurons drive wakefulness via wake-promoting neurons.
- OX2Rs in the TMN drive long wake bouts.
- OX1Rs in the LC maintain wakefulness. Inhibition of LC reduces wakefulness.



BF = basal forebrain
TMN = Tuberomammillary nucleus
PPT-LDT = Pedunculopontine and lateral dorsal tegmental nucleus
DR=Dorsal raphe
LC=Locus ceruleus

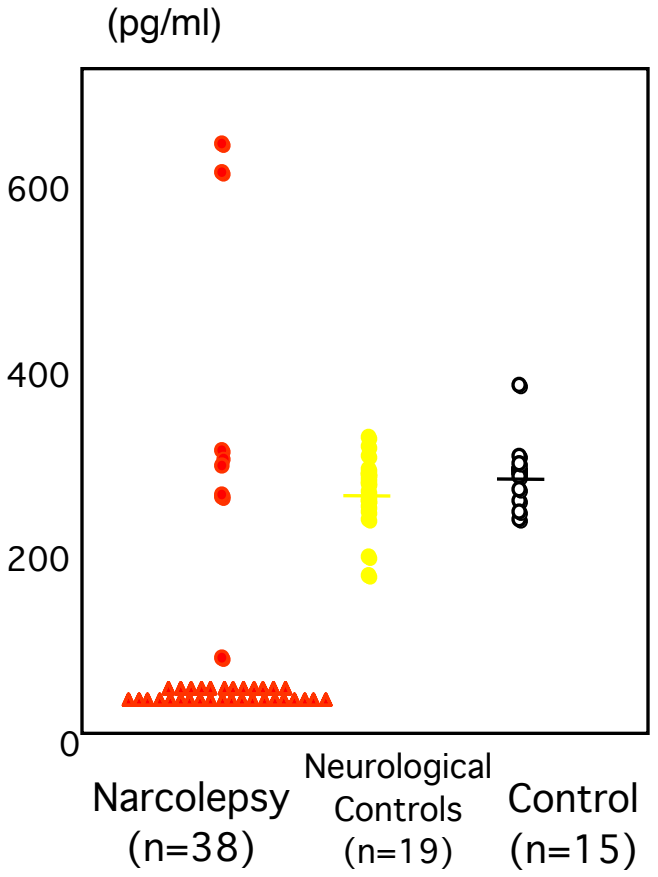
OREXIN PATHWAYS

- Medial prefrontal cortex (MPFC). Lack of orexin neurons reduce activity of ventrolateral periaqueductal gray-lateral pontine tegmentum (vlPAG-LPT) and dorsal raphe-locus ceruleus (DR-LC).
- Emotions via the amygdala strongly inhibits the vlPAG/LPT, enabling the sublaterodorsal tegmental nucleus (SLD). SLD drives muscle paralysis through GABA inhibition of motor neurons thereby resulting in cataplexy.

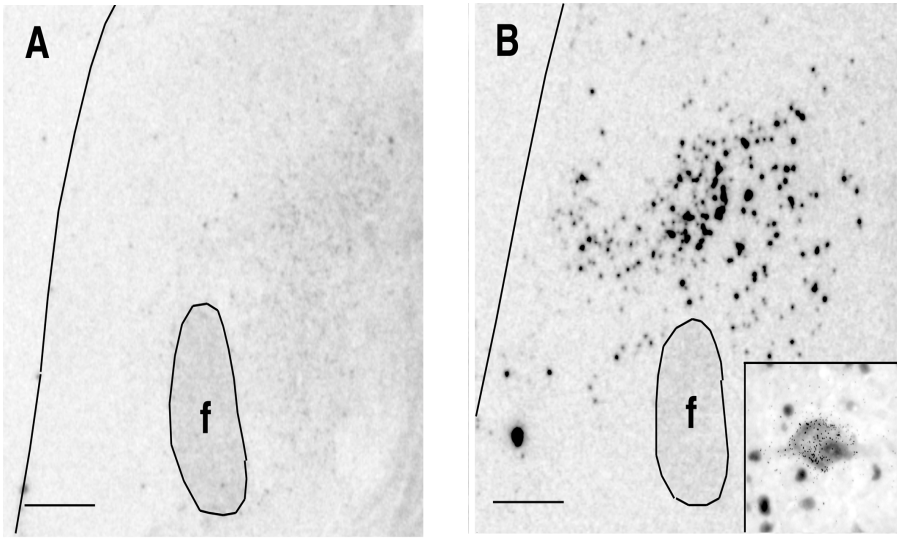


OREXIN ABSENT IN CSF AND THE BRAIN

Cerebrospinal Fluid



Lateral Hypothalamic brain tissue



Narcoleptic

Control

Adapted from Nishino S et al, Lancet 2000;355 and Peyron C et al, Nat Med 2000;6.

OVERVIEW

- Characteristics
- Assessment, Evaluation, and Diagnosis

CLINICAL FEATURES

- Excessive daytime sleepiness
- Hypnagogic hallucinations
- Sleep paralysis
- Cataplexy
- Disrupted/Fragmented nocturnal sleep
- Other associated features (e.g., depression, headaches, psychosocial problems)

Tetrad

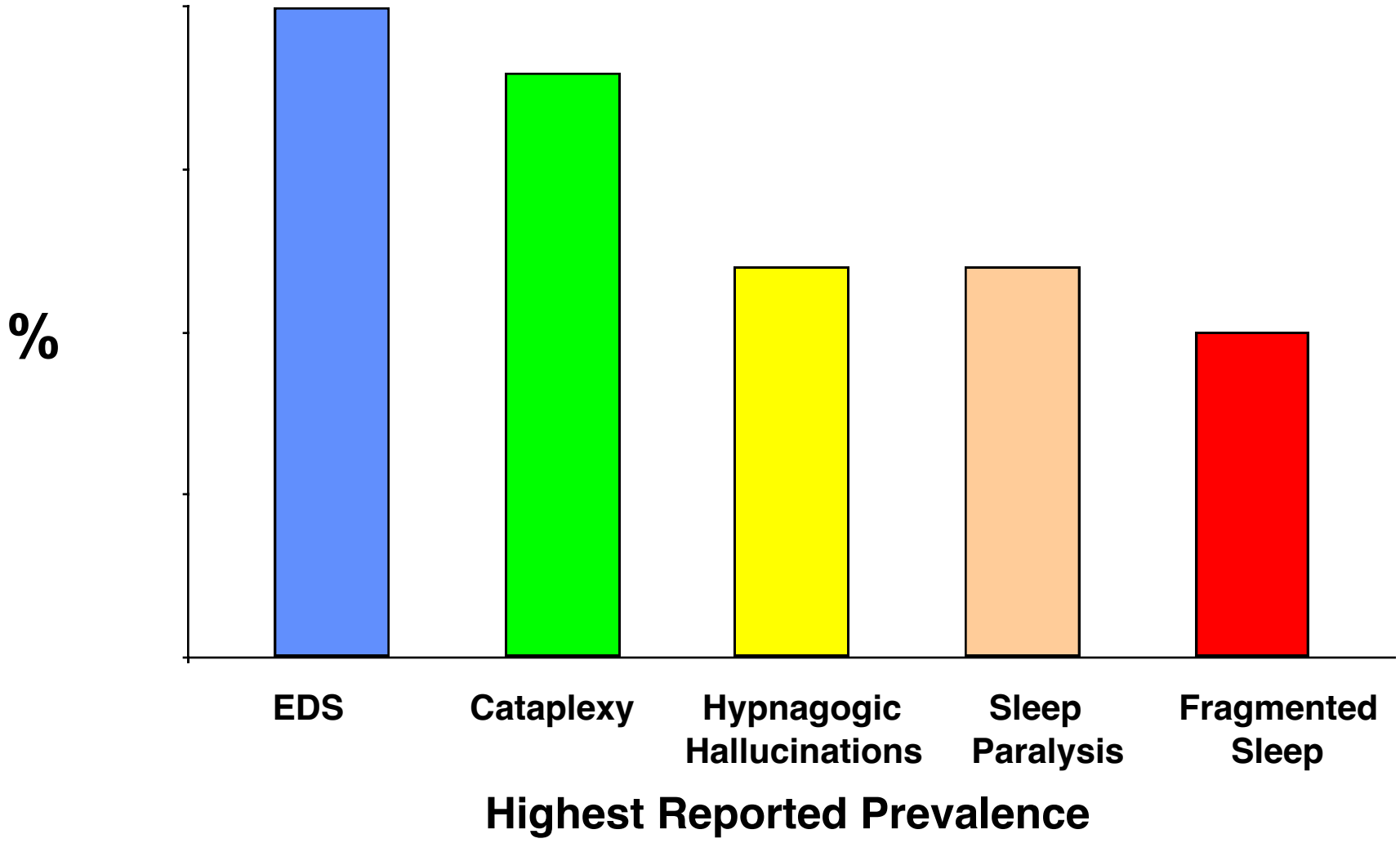
Pentad

Yoss RE, Daly DD. Criteria for the diagnosis of the narcoleptic syndrome. Proc Staff Meet Mayo Clin 1957;32:320-328.

SYMPTOM ONSET

- Excessive daytime sleepiness and sleep attacks are usually the initial symptoms
- Cataplexy may rarely antedate other symptoms but may occur up to 20 years later, though it most often occurs within a year of onset of daytime sleepiness

SYMPTOM PREVALENCE



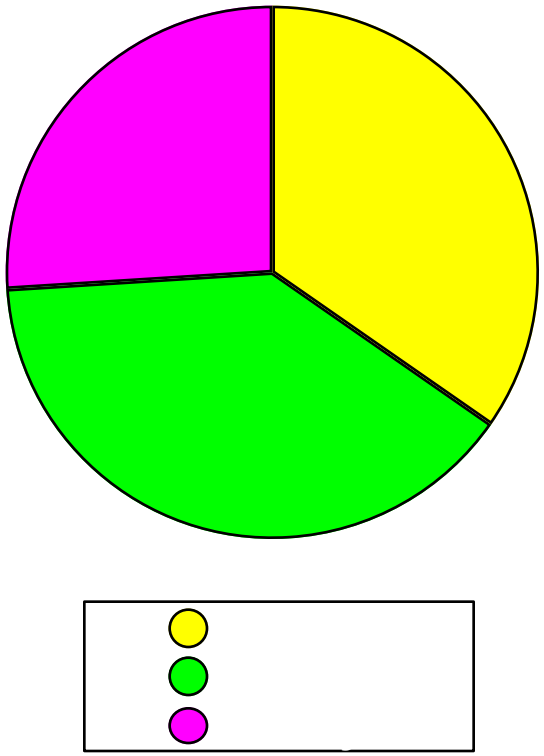
Sleep Academic Award Program, NHLBI and AASM-Adapted from Honda Y. Clinical features of narcolepsy: Japanese experience. In: Honda Y, Juji T, eds. HLA in Narcolepsy. Tokyo: Springer-Verlat, 1988:24-57.

EXCESSIVE DAYTIME SLEEPINESS

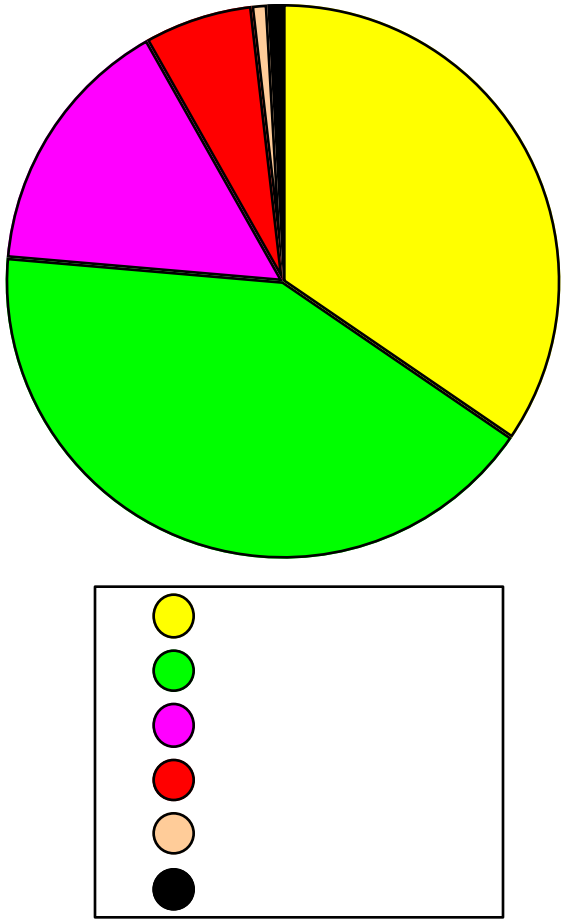
- Attacks of sleepiness recur throughout the day during a wide spectrum of activities
- Refractory periods of feeling refreshed from one to several hours following naps
- May have persistent drowsiness throughout the day with automatisms and decreased concentration, performance, short-term memory
- Associated with fragmented sleep

EXCESSIVE DAYTIME SLEEPINESS

Frequency of Daytime Sleep Episodes



Reported Duration of Daytime Naps



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SLEEPINESS VS. FATIGUE

- Conceptual framework
- Diagnostic strategies
- Classification of sleep disorders

FATIGUE SEVERITY SCALE

During the past week, I have found that:

	Strongly Disagree			Neither Agree Nor Disagree			Strongly Agree
1. My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
2. Exercise brings on my fatigue.	1	2	3	4	5	6	7
3. I am easily fatigued.	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
8. Fatigue is among my three most disabling symptoms.	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7

Krupp, L. B., LaRocca, N. G., Muir-Nash, J., & Steinberg, A. D. (1989). The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. Archives of Neurology, 46 , 1121–1123.

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SLEEPINESS ASSESSMENT

- Stanford Sleepiness Scale and Epworth Sleepiness Scale
- Narcolepsy Severity Scale and Swiss Narcolepsy Scale
- Pupillography
- Multiple Sleep Latency Test (MSLT)
- Maintenance of Wakefulness Tests (MWT)
- Continuous polygraphic monitoring

SLEEPINESS SCALES

- Questionable reliability with chronic sleepiness
- Epworth Sleepiness Scale (ESS) limited to adults and restricted life situations
- ESS and Stanford Sleepiness Scale may not correlate with objective measures of sleepiness

STANFORD SLEEPINESS SCALE

The subject is to choose the statement that best describes his/her state.

1. Feeling active and vital, alert, wide awake
2. Functioning at high level, but not at peak, able to concentrate
3. Relaxed, awake, not at full alertness, responsive
4. A little foggy, not at peak, let down
5. Fogginess, beginning to lose interest in remaining awake, slowed down
6. Sleepiness, prefer to be lying down, fighting sleep, woozy
7. Almost in reverie, sleep onset soon, lost struggle to remain awake

Hoddes E, et al. Psychophysiology. 1973 Jul;10(4):431-6

EPWORTH SLEEPINESS SCALE

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? 0 = would *never* doze, 1= *slight* chance of dozing, 2 = *moderate* chance of dozing, 3 = *high* chance of dozing

	Chance of Dozing
Sitting and Reading	_____
Watching TV	_____
Sitting inactive in a public place (meeting, theater, etc.)	_____
As a passenger in a car for 1 hour without a break	_____
Lying down in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

Total

Johns MW. *Sleep, 14*(6):540-545, 1991

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NARCOLEPSY SCALES

SWISS NARCOLEPSY SCALE (SNS)

- Validated self-report scale to assess sleepiness
- On a 5 item, 5-point scale, patients rate the frequency of individual symptoms (excessive daytime sleepiness and cataplexy)
- Each answer is weighted by a positive or negative factor; score of < 0 is suggestive of narcolepsy with cataplexy
- The SNS has a high sensitivity and specificity in identifying NT1 (particularly compared to ESS)
- A two-item short form version (sSNS) also available demonstrating discriminative power for NT1

NARCOLEPSY SEVERITY SCALE (NSS)

- Validated self-report scale to assess narcolepsy severity
- The NSS consists of 15 items that cover symptoms of the narcolepsy pentad
- Each item is rated on a scale of 0 to 6 (for frequency) or 0 to 4 (for impact on daily life). Total score ranges from 0 to 57, with higher scores indicating greater severity.
- The scale demonstrates good reliability and discriminant validity; it is used for quantifying narcolepsy symptoms, monitoring and optimizing treatment management, and assessing the severity and consequences of narcolepsy symptoms

Bassetti CL. Spectrum of narcolepsy. In: Baumann CR, Bassetti CL, Scammell TE, eds. Narcolepsy: Pathophysiology, Diagnosis, and Treatment. New York, NY: Springer Science+Business Media; 2011:309-319.
Sturzenegger C, Bassetti CL. The clinical spectrum of narcolepsy with cataplexy: a reappraisal. J Sleep Res. 2004;13(4):395-406.

Dauvilliers Y, et al. Measurement of narcolepsy symptoms: The Narcolepsy Severity Scale. Neurology. 2017 Apr 4;88(14):1358-1365.

MULTIPLE SLEEP LATENCY TEST

- Four or five scheduled 20-minute naps separated by 2 hours
- An MSLT with a mean sleep latency of less than 8 minutes and 2 or more sleep-onset REM periods is diagnostic for narcolepsy
- Patients should be non-sleep deprived; off stimulants, stimulant-like medications, and REM-suppressing medications for 2 weeks; and their sleep should be stable without evidence of other disorders.

MULTIPLE SLEEP LATENCY TEST

- 84% of narcoleptic patients had 2 or more SOREMPs on single-day MSLTs
- Individuals with 2 or more SOREMPs on MSLTs and excessive daytime sleepiness may develop cataplexy many years later
- 85% of narcoleptics with 2 or more SOREMPs have SOREMPs of less than 5 minutes
- A mean sleep latency of 3.1 ± 2.9 minutes was found in narcoleptics by a meta-analysis
- 24/100 of OSA patients had a positive MSLT

CONTINUOUS POLYGRAPHIC MONITORING

- 24 to 36 hours
- Can capture microsleeps and cataplectic attacks
- Not a routine or accepted procedure for narcolepsy diagnosis

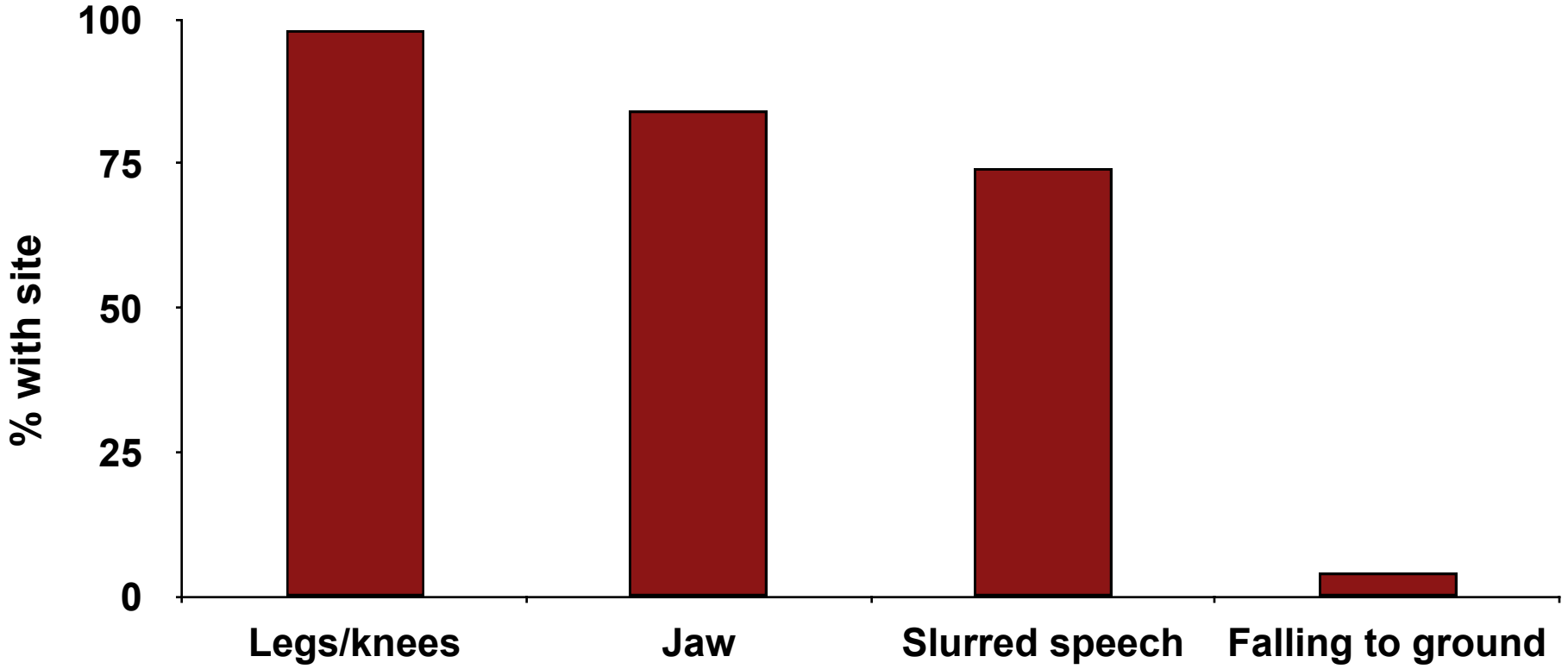
HYPNAGOGIC HALLUCINATIONS AND SLEEP PARALYSIS

- Vision or auditory hallucinations are common
- Abnormal feelings in the extremities, levitation or extracorporeal sensations are not rare
- Extreme anxiety often accompanies the paralysis

CATAPLEXY

- Sudden decrement in muscle tone often precipitated by emotion, stress, fatigue, or meals
- Commonly involves postural muscles
- Lasts seconds to minutes
- Blurred vision, speech difficulty, irregular respiration may be present
- Monosynaptic stretch reflexes are suppressed

SITES OF CATAPLEXY



Sleep Academic Award Program, NHLBI and AASM-Adapted from Anic-Labat S, Guilleminault C, Kraemer HC, Meehan J, Arrigoni J, Mignot E. Validation of a cataplexy questionnaire in 983 sleep-disorders patients. SLEEP 1999;22(1):77-87.


1995 12 22

AMERICAN HEART ASSOCIATION (AHA) LIFE'S ESSENTIAL 8

AHA Cardiovascular Health Checklist: Determinants of Cardiovascular Health

- ✅ **Sleep duration**
- ☑ **Physical activity**
- ☑ **Body mass index**
- ☑ **Diet**
- ☑ **Blood pressure**
- ☑ **Blood glucose**
- ☑ **Blood lipids**
- ☑ **Nicotine exposure**

7 to 9 hours of nightly sleep for optimal cardiovascular health for adults, and more for children depending on age.

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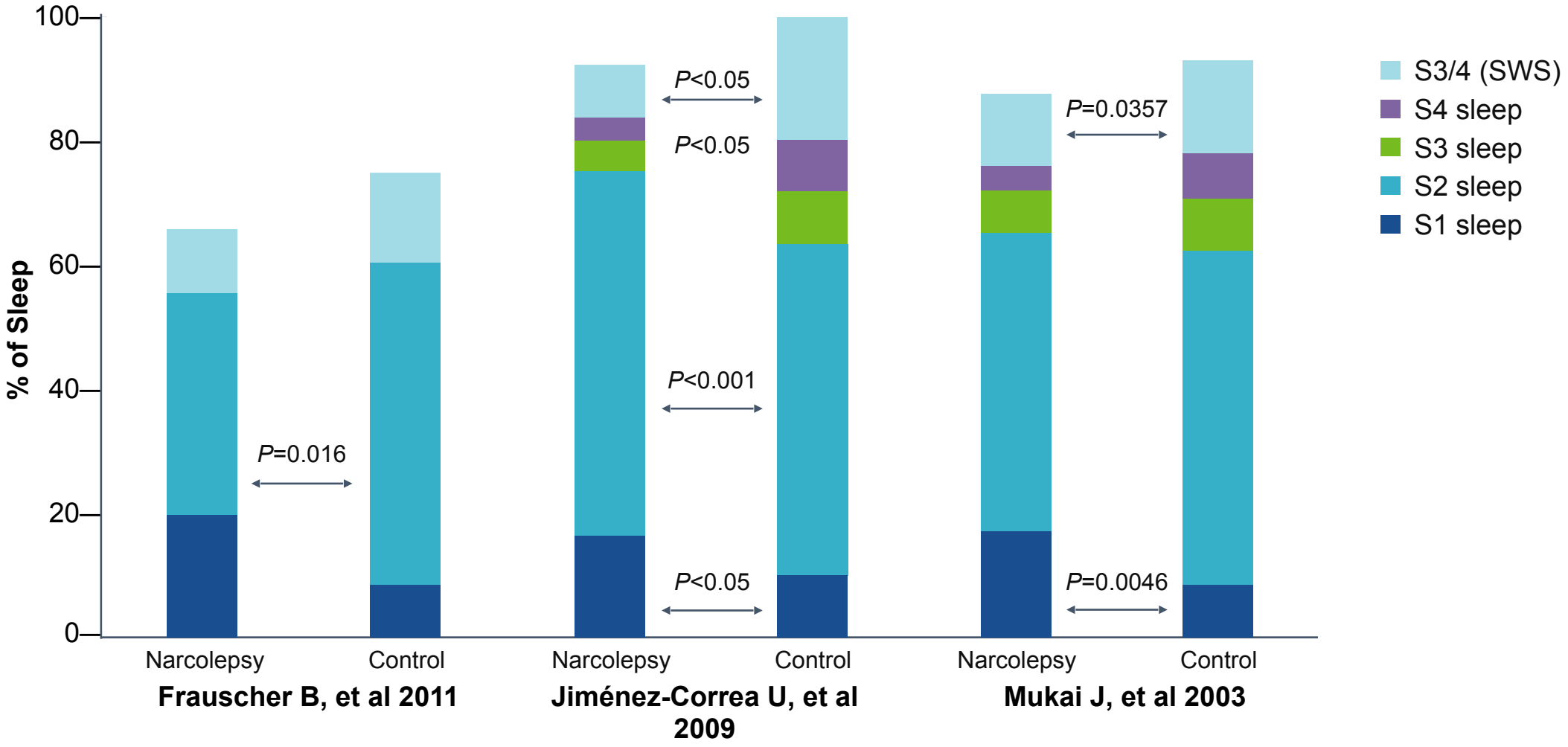
DISRUPTED NOCTURNAL SLEEP



S1, stage 1; S2, stage 2; S3, stage 3; S4, stage 4; SWS, slow wave sleep. Frauscher et al.,[23] Jiménez-Correa et al.,[26] Mukai et al.[30]

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Arousals and Wake After Sleep Onset Identified by PSGs

	Arousal Index		Number of Arousals		Wake After Sleep Onset	
Study	**Patients With Narcolepsy**	**Normal Controls**	**Patients With Narcolepsy**	**Normal Controls**	**Patients With Narcolepsy**	**Normal Controls**
Frauscher B, 2011	21.6	8.7[a]	–	–	41.3 min	33.1 min
Jiménez-Correa U, 2009	–	–	78.38	59.13[b]	–	–
Mukai J, 2003	–	–	–	–	3.9%	1.0%[b]
Khatami R, 2007	–	–	–	–	31.5 min	10.4 min[c]
Khatami R, 2008	–	–	–	–	39.5 min	11.2 min[d]

[a]*P*=0.004. [b]*P*<0.05. [c]*P*<0.01. [d]*P*=0.00.

Compared to normal controls, narcolepsy patients experienced significantly more sleep disruptions and longer WASO periods

DNS, disrupted nighttime sleep; WASO, wake after sleep onset.

Roth T, et al., Disrupted Nighttime Sleep in Narcolepsy *J Clin Sleep Med*. 2013;9(9):955-965

DISRUPTED NOCTURNAL SLEEP

- International panel of experts convened in 2011 to build consensus among experts incorporating both clinical experience and comprehensive literature review: disrupted nocturnal sleep was found to range from 30% to 95%. [1]
- 60.8% of untreated patients and 40.3% of treated patients experienced nighttime sleep disturbance, as assessed by the Narcolepsy Severity Scale (NSS).[2]
- AASM added DNS in the International Classification of Sleep Disorders in 2014 (ICSD-3), which was described as an inability to maintain continuous sleep

(1) Roth T, et al. J Clin Sleep Med. 2013. (2) Dauvilliers Y, et al. *Sleep*. 2020

REM SLEEP ABNORMALITIES

- Sleep-onset REM periods (SOREMPs) are frequent during the daytime.
- Visual and auditory hypnagogic/hypnopompic hallucinations can occur (40-80%).
- Frequent, vivid, frightening and bizarre dreams, nightmares, lucid dreams, delusional dreams, out-of-body experiences and dreams of flying often occur.
- Sleep paralysis can with dreams or hallucinations (40-80%).
- REM sleep behavior disorder (RBD), which can cause of bodily injury to the patient and/or bed partner, can occur in up to 60% of those with NT1.

Ahmed I, Thorpy M. Clinical features, diagnosis and treatment of narcolepsy. Clin Chest Med. 2010 Jun;31(2):371-81.

NARCOLEPSY DIAGNOSIS

- ❑ Initial History and Physical Examination
- ❑ Sleep Log / Diary
- ❑ Actigraphy
- ❑ Overnight PSG and MSLT
- ❑ Maintenance of Wakefulness Test (MWT)
- ❑ CSF hypocretin-1 levels

Sateia MJ. *Chest.* 2014;146(5):1387-1394. Sansa G, et al. *Sleep Med*. 2010;11(1):93-95. Black J, et al. *Sleep Med*. 2017;33:13-18. Maski K, et al. *J Clin Sleep Med*. 2017;13(3):419-425.

NARCOLEPSY TYPE 1 VS. NARCOLEPSY TYPE 2 (ICSD-3)

Narcolepsy Type 1 (NT1)
(Narcolepsy with Cataplexy)
A and B must be met

A. EDS ≥ 3 months
B. At least one of the following:
   - Cataplexy and a positive MSLT
     - Low mean sleep latency ≤ 8 mins
     - ≥ 2 SOREMPs on MSLT-PSG
   - Low CSF hypocretin-1 concentration (≤ 110pg/ml or < 1/3 of normal)

Narcolepsy Type 2 (NT2)
(Narcolepsy without Cataplexy)
A-E must be met

A. EDS ≥ 3 months
B. Positive MSLT
   - Low mean sleep latency ≤ 8 mins
   - ≥ 2 SOREMPs on MSLT-PSG
C. Cataplexy is absent
D. CSF hypocretin-1 concentration > 110pg/ml or > 1/3 of normal
E. Hypersomnolence and MSLT findings not better explained by other causes:
   - Insufficient sleep, OSA, delayed sleep phase, drug intake/withdrawal

DISTINGUISHING FEATURES: TYPE 2 NARCOLEPSY WITHOUT CATAPLEXY

- Represents 10-50% of the narcoleptic population
- Approximately 40% are HLA DQB1*0602 positive vs. 12-25% of controls
- 10-20% of patients without cataplexy (almost all with HLA DQB1*0602) have decreased CSF hypocretin-1 levels ≤ 110 pg/mL

DIFFERENTIAL DIAGNOSIS

EXCESSIVE DAYTIME SLEEPINESS

- Other Hypersomnias
- Other Sleep-Wake Disorders (e.g., Obstructive Sleep Apnea and Periodic Limb Movement Disorder, Circadian Rhythm Sleep-Wake Disorders)
- Sleep Loss or Deprivation
- Poor Sleep Habits/Hygiene
- Medical Disorders (e.g., Thyroid Disease)
- Mood Disorders
- Substance Use

CATAPLEXY

- Seizures
- Syncopal Episodes
- Psychogenic

HALLUCINATIONS

- Schizophrenia
- Sleep Terrors

Nevsimalova S. *Curr Neurol Neurosci Rep*. 2014;14(8):469. Warman J, et al. *Neurology*. 2013;80(7 Suppl):S43.003. Dauvilliers Y, et al. *Neurol Neurosurg Psychiatry.* 2003;74(12):1667-1673. Zhou J, et al. *Shanghai Arch Psychiatry.* 2014; 26(4):232-235.

HYPERSOMNIAS

- Idiopathic Hypersomnia
- Recurrent Hypersomnia (Kleine-Levin Syndrome)
- Hypersomnia Due to a Medical Disorder
- Hypersomnia Due to a Medication or Substance
- Hypersomnia Associated with a Psychiatric Disorder
- Insufficient Sleep Syndrome

Idiopathic Hypersomnia Diagnostic Criteria

A-F must be met

A. EDS ≥ 3 months
B. Cataplexy is absent
C. < 2 SOREMPs on MSLT-PSG
D. At least one of the following:
   - Low MSLT mean sleep latency ≤ 8 mins
   - Total 24-hour sleep time ≥ 660 minutes (12-14 hours) on 24-hour PSG monitoring or by wrist actigraphy in association with a sleep log (averaged over ≥ 7 days)
E. Insufficient sleep syndrome is ruled out
F. Hypersomnolence and MSLT findings not better explained by other causes:
   - Another sleep disorder, other medical or psychiatric disorder, or use of drugs or medications

DIAGNOSTIC CRITERIA: RECURRENT HYPERSOMNIA

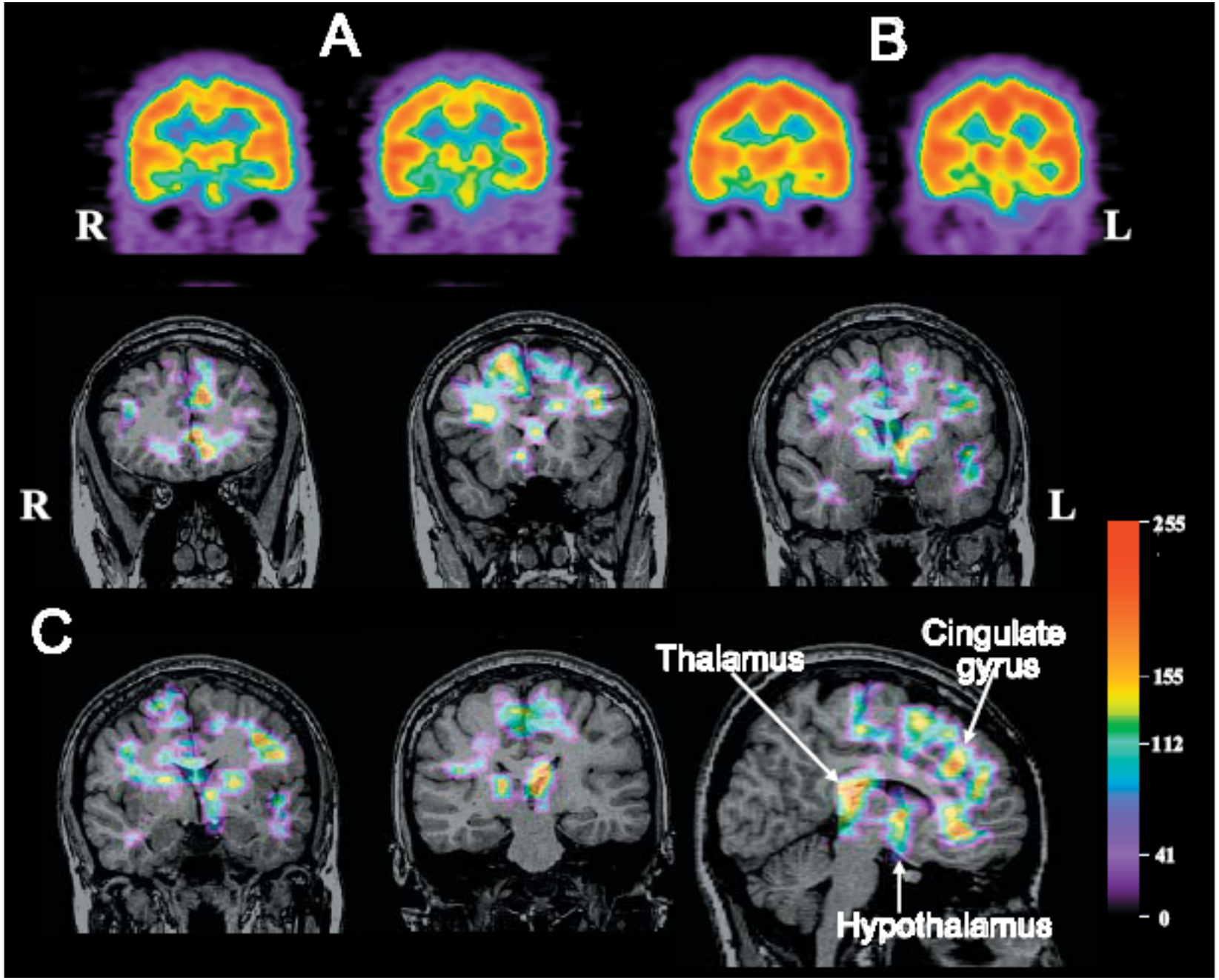
Includes Kleine-Levin Syndrome and Menstrual-Related Hypersomnia

- At least 2 recurrent episodes of excessive sleepiness and sleep duration, each persisting for 2 days to 5 weeks
- Episodes recur at least once a year and ≥ once every 18 months
- The patient has normal alertness, cognitive functioning and behavior between attacks

KLEINE-LEVIN SYNDROME

- Sleep episodes approaching 24 hrs/day and may occur 12 times/year
- Irritability and depression can occur, as well as confusion, amnesia, and abnormal speech
- Cognitive dysfunction, altered perceptions, increased appetite, hypersexuality, and aggressive behavior are common
- Most frequent in adolescents, with a male predominance

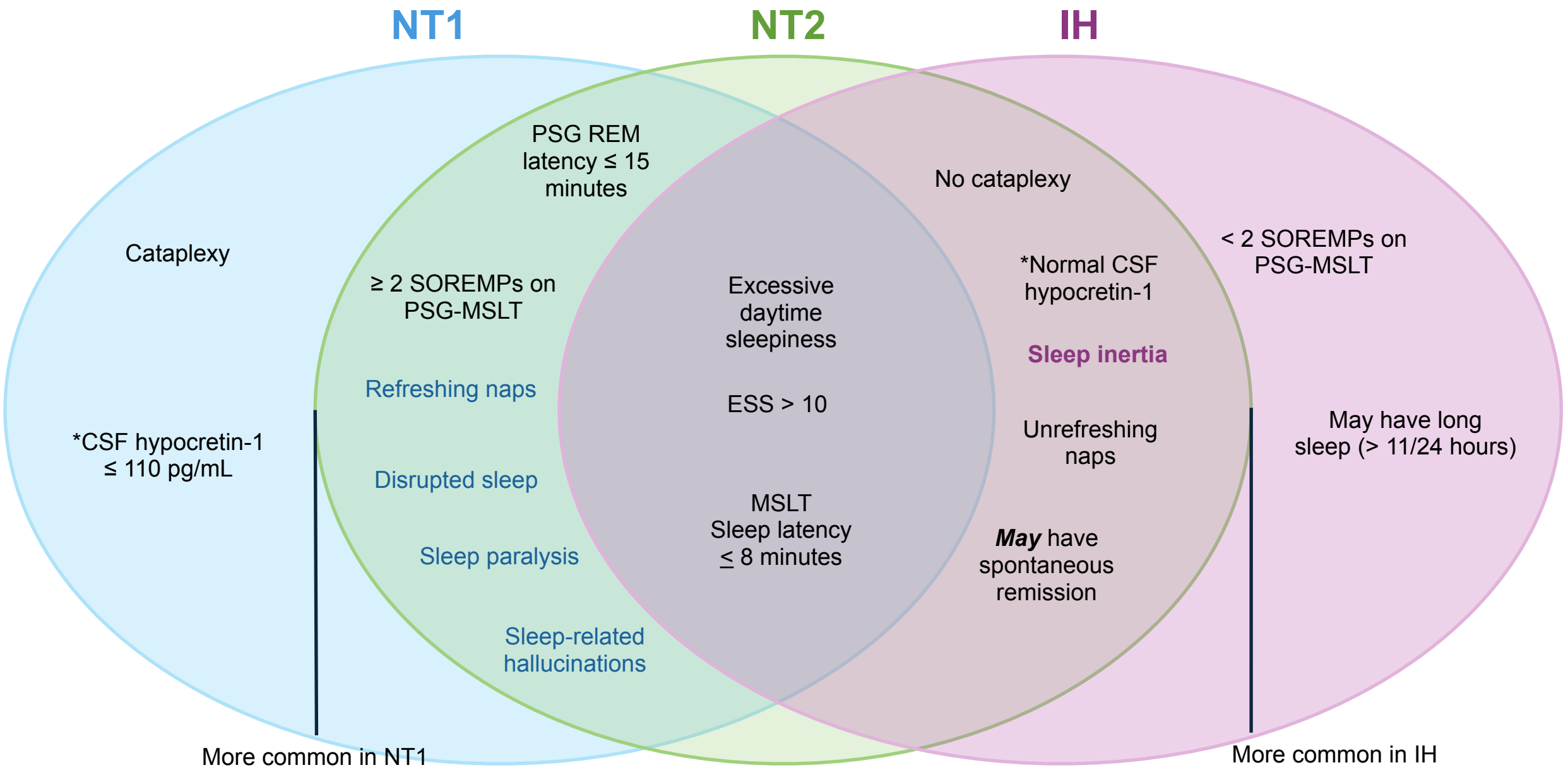
KLEINE-LEVIN SYNDROME



Single photon emission computed tomography (SPECT) during a symptomatic period and subtraction analysis between symptomatic and asymptomatic periods shows hypoperfusion in bilateral frontal regions, temporal lobes, thalamus, and hypothalamus

Hong, et al. *SLEEP* 2006; 29(8):1091-3.

DIFFERENTIATING NARCOLEPSY TYPE 1 AND TYPE 2 FROM IH



IH = idiopathic hypersomnia; REM = rapid eye movement *CSF hypocretin-1 is also known as orexin-A

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