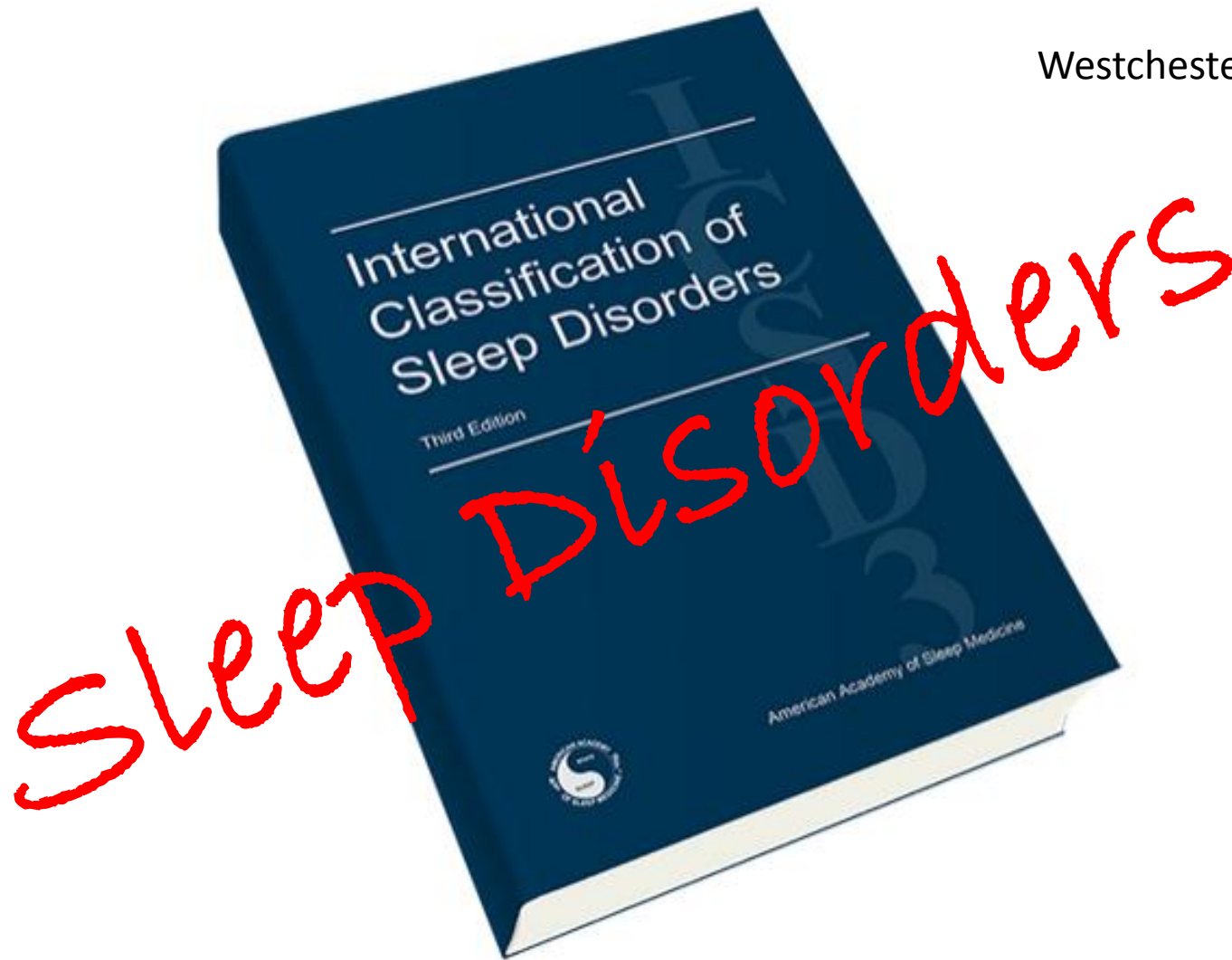


Westchester, 2014



International Classification of Sleep Disorders, 2014 (ICSD-3)

1. **INSOMNIA**
2. **SLEEP-RELATED BREATHING DISORDERS**
3. **CENTRAL DISORDERS OF HYPERSOMNOLENCE**
4. **CIRCADIAN RHYTHM SLEEP-WAKE DISORDERS**
5. **PARASOMNIAS**
6. **SLEEP RELATED MOVEMENT DISORDERS**
7. **OTHER SLEEP DISORDER**

- **Hypersomnolence**= Daytime sleepiness= the inability to stay awake and alert during the major waking episodes of the day, resulting in periods of irrepressible need for sleep or unintended lapses into drowsiness or sleep
 - variable severity
 - Mild: in sedentary, boring, and monotonous situations that require little active participation
 - Moderate: pt. awares of increasing sleepiness before falling asleep
 - Severe: pt. falls asleep with little or no prodromal symptoms (“sleep attacks”)
- **Hypersomnia**= disorder with hypersomnolence

International Classification of Sleep Disorders, 2014 (ICSD-3)

CENTRAL DISORDERS OF HYPERSOMNOLENCE

1. Narcolepsy Type 1
2. Narcolepsy Type 2
3. Idiopathic Hypersomnia
4. Kleine-Levin Syndrome
5. Hypersomnia Due to a Medical Disorder
6. Hypersomnia Due to a Medication or Substance
7. Hypersomnia Associated with a Psychiatric Disorder
8. Insufficient Sleep Syndrome

Narcolepsy Type 1

- **Alternate Names:** Hypocretin deficiency syndrome, **narcolepsy-cataplexy**, narcolepsy with cataplexy
- **Essential features:**
 - **Excessive daytime sleepiness with irresistible sleep attacks**
 - **Cataplexy**
- **Associated Features**
 - **Disruption of nocturnal sleep**, an inability to maintain continuous sleep
 - **Hypnagogic/ Hypnopompic hallucinations**
 - vivid dreamlike experiences occurring at the transition from wake to sleep or at sleep to wake transitions.
 - multimodal or “holistic” character, often combining visual, auditory, and tactile phenomena.
 - **Sleep paralysis**
 - disturbing temporary inability to move voluntary muscles at sleep-wake transitions. Despite being awake and conscious of the sleeping environment, it is impossible for subjects to move their limbs or even open their eyes. The experience may last for several minutes.
 - **Obesity**
 - An increased frequency of several **other sleep abnormalities**
 - sleep talking
 - periodic limb movements of sleep
 - sleep disordered breathing
 - REM sleep behavior disorder

NARCOLEPSY

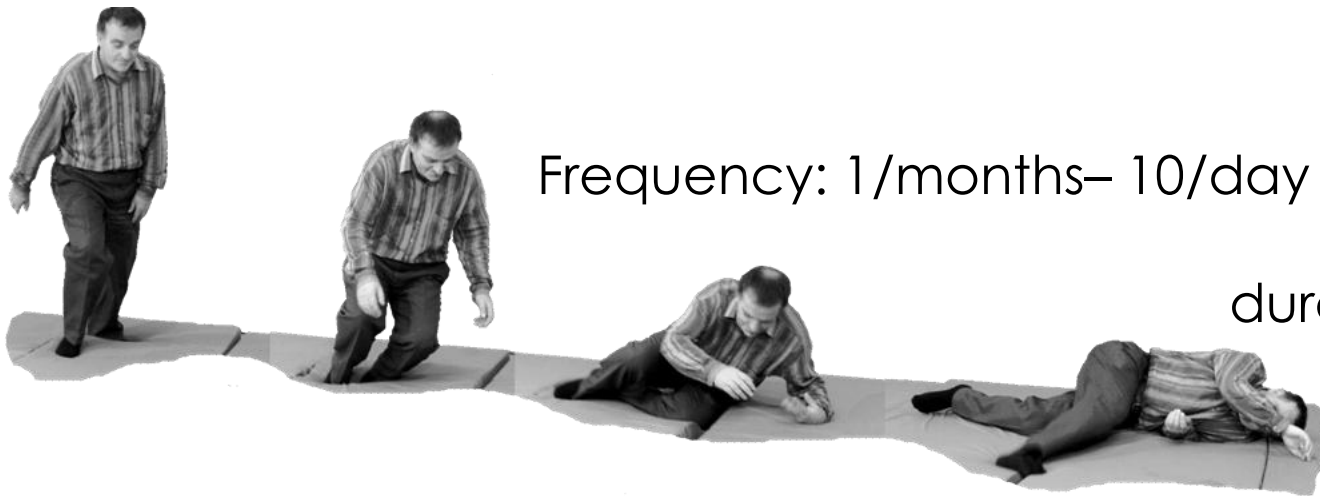
Cataplexy

A sudden, bilateral loss of muscle tone, with preserved consciousness, triggered by emotions (laughing, anger, excitement)

Rarely: excessive sports, anticipation

Frequency: 1/months– 10/day

duration: 1-2 min



NARCOLEPSY

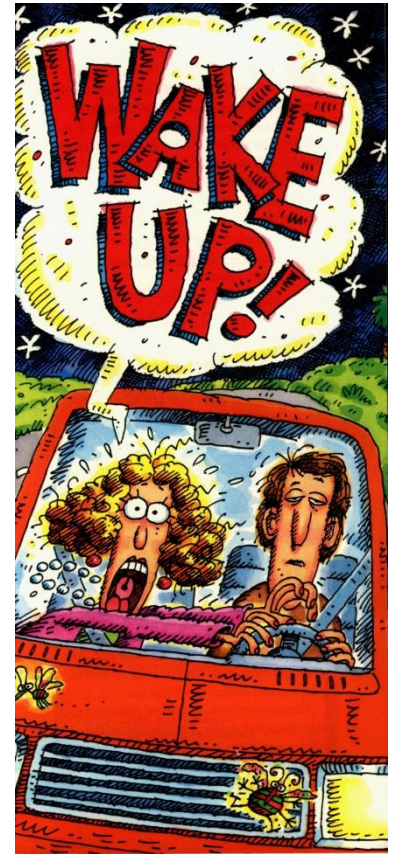
Diagnosis of cataplexy

- Diagnosis of cataplexy crucial to diagnose narcolepsy
- In combination with EDS it is pathognomonic
- Cataplexy usually first occurs after the appearance of EDS
- Isolated cataplexy is very rare
 - All skeletal muscles can be involved
 - Exception: eye-movements and respiration
 - Complete versus partial attacks
 - Partial attacks: neck, jaw, knees



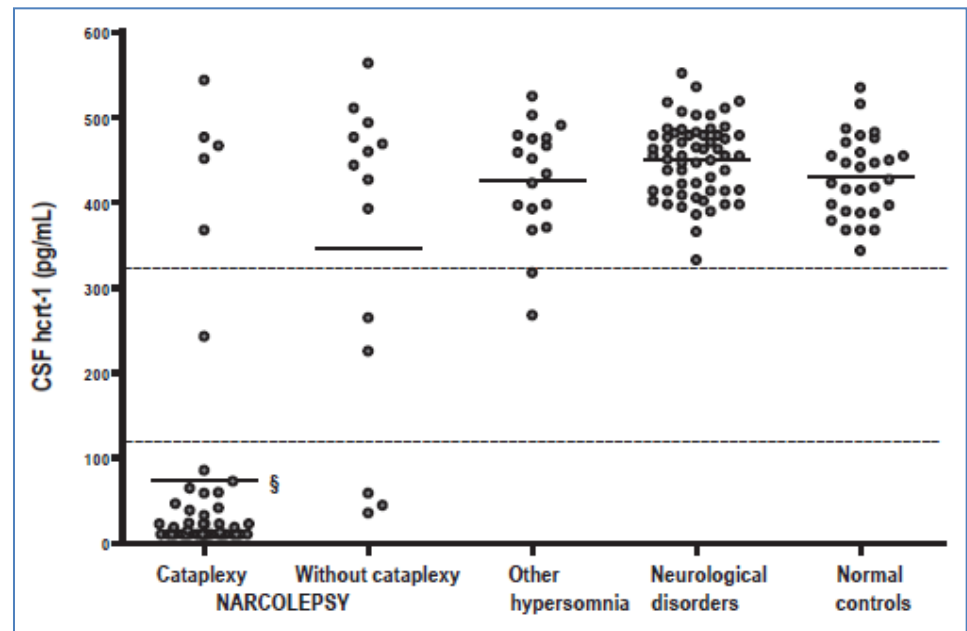
Traffic accidents

- 25-36% of all narcolepsy patients have accidents
- The number of accidents caused by sleepiness is 7x higher than in controls
- Accidents caused by cataplexies are reported by 50% of all narcolepsy patients
- The incidence of narcolepsy patients per year is not higher than in controls



Narcolepsy Type 1

- HLA class II typing: **DQB1*0602**
- **CSF-hcrt-1** is a valid method when using reference samples from referral centers (<30% of mean value)
- It is recommended in unclear cataplexy or PSGs, and in patients not being able to tolerate PSG



Narcolepsy Type 1

- hypocretin deficiency syndrome- **selective loss** of hypothalamic hypocretin producing neurons

- strong HLA association in narcolepsy
- Association with gen polymorphism for
 - T-cell receptor alfa (TCR)
 - Purinergic receptor P2RY11
- autoantibodies against
 - Tribbles homolog 2 (TRIB2)
 - ASLO

Vaccination against H1N1

**autoimmune
process**

Narcolepsy Type 1

Diagnostics

- ✓ Medical history
 - ✓ HLA
 - ✓ PSG, MSLT
 - ✓ CSF –hcrt-1 in unclear cases of cataplexy, pts. not able to tolerate PSG
- histamine

Narcolepsy Type 1

Treatment

- Causal: 0
- Symptomatic
 - Excessive daytime sleepiness
 - Stimulants: Amfetamín, Metamfetamín, Dexamfetamín, Metylfenidát, **Modafinil**
 - Cataplexy
 - Tricyclic antidepressants
 - SSRI, NSRI
 - Excessive daytime sleepiness + Cataplexy
 - **GAMMA-HYDROXY BUTYRÁT**® XYREM

5. Parasomnias

- **NREM parasomnias**
 - Confusional Arousals
 - Somnambulism
 - Sleep Terror
- **REM parasomnias**
 - REM Behavior Disorder
 - Nightmare Disorder
- **Other Parasomnias**
 - Sleep Enuresis
 - Exploding Head syndrome

10% children
Familial distribution
Risk of injury
Amnesia in the morning

Adults over 60 yy
Younger cases are secondary to
narcolepsy, SSRI,...
Injuries
„idiopathic“ later progress to
synucleopathies (PD, MSA, LBD)

REM Behavior Disorder

PSG: Loss of REM atonia

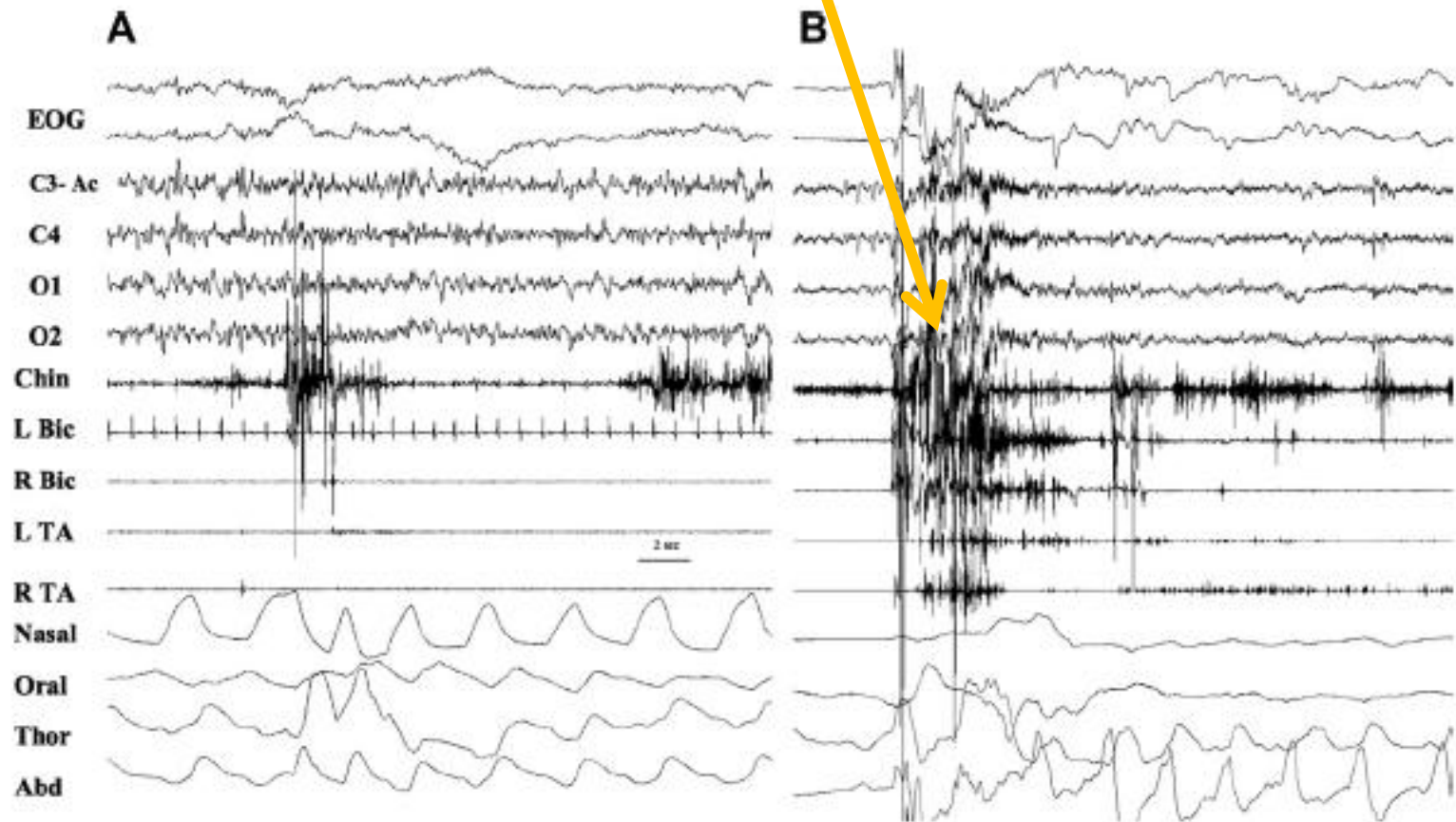


Fig. 2. A) Excessive phasic electromyographic activity and intermittent increased tonic electromyographic activity in the chin with normal atonia in the limbs during REM sleep in a patient with RBD. B) Abnormal phasic electromyographic burst of all the muscles recorded associated with a sudden body jerk during REM sleep in a patient with RBD. (Abbreviations as in Fig. 1).

Treatment: Clonazepam

6. SLEEP RELATED MOVEMENT DISORDERS

Diagnostic criteria for Restless Legs Syndrome (RLS) *Essential features*

- 1) An urge to move the legs
- 2) that is present at rest
- 3) relieved by movement, and
- 4) demonstrates a circadian pattern with peak symptoms occurring at night or in the evening

Allen et al Sleep Med 2003

6. SLEEP RELATED MOVEMENT DISORDERS

Diagnostic criteria for

Restless Legs Syndrome (RLS)

Non essential but common features

- Family history
- Response to dopaminergic therapy
- Experience of PLM during sleep or during wakefulness
- Sleep disturbance
- An increase in severity with advancing age

Etiopathogenetic Hypotheses in RLS

- **CNS dysfunction**
- **Iron system abnormalities**
- **Genetic factors**
- **Dopamine system abnormalities**

CNS Dysfunction

- There is no evidence of systematic structural abnormalities of the brain in RLS patients, as shown by standard MRI or autopsy

Paulus W et al, Mov Disord 22: 1451-56, 2007

- Only an MRI study by use of voxel-based morphology technique showed a significant grey matter decrease in the primary somatosensory cortices of both hemispheres in RLS patients

Unrath A et al, Mov Disord 22: 1751-56, 2007

The role of iron in RLS

R. Allen and C. Earley

Mov Disord, 2009

There are 3 **major secondary causes** of RLS:

- *Iron deficiency*
- *End-stage renal disease*
- *Pregnancy*

In each of these conditions there is a higher than expected prevalence of RLS, that commonly resolves when the condition is corrected

They all compromise **iron sufficiency**

Dopamine and RLS

- The rapid and dramatic improvement of RLS with dopaminergic treatment is the strongest argument in favour of dopaminergic system involvement in the pathogenesis of RLS

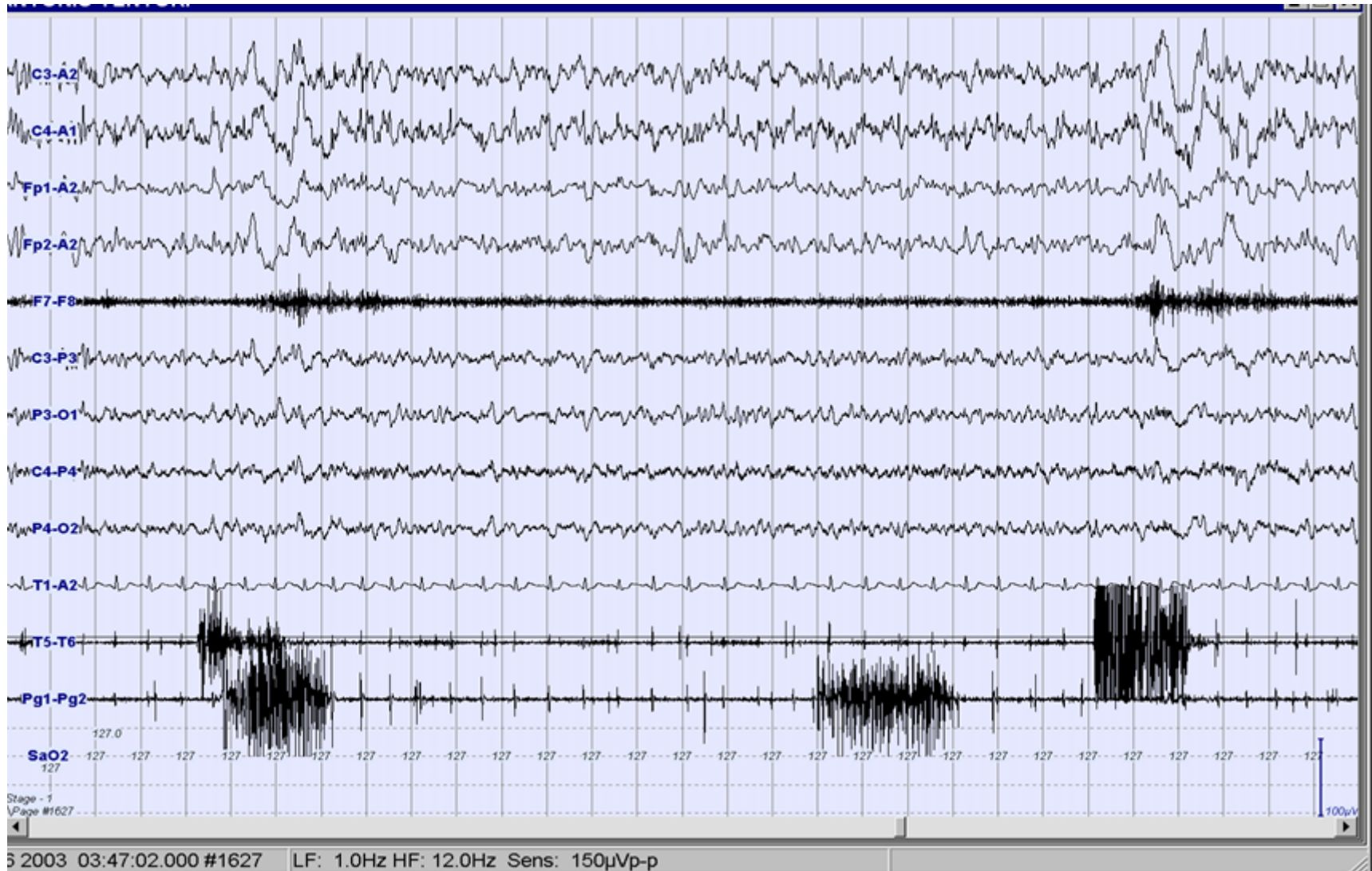
Merlino G et al, Neuropsychobiology 54: 195-200, 2006

Manconi M et al, Sleep Med 8: 491-7, 2007


RLS- diagnostics

- Sleep history
- Personal history
- Laboratory screening
 - PSG, actigraphy

PERIODIC LEGS MOVEMENTS (PLMs)



RLS- treatment

- Primary RLS
 - Dopaminergic stimulation
 - Levodopa/carbidopa
 - Pramipexol, Ropinirol, Rotigotin
 - Gabapentin, Pregabalin 
- Secondary cases
 - Fe supplementation
 - Treatment of underlying condition

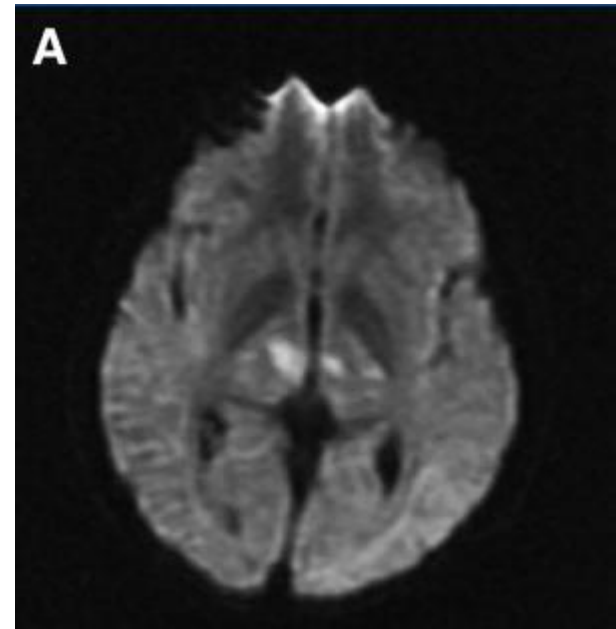
BISS = Behaviorally induced insufficient sleep syndrome

Diagnostic Criteria

- A. Complaint of excessive daytime sleepiness, at least 3 months
- B. Habitual sleep episode (history, sleep log, or actigraphy) is usually shorter than from age-adjusted normative data
- C. At weekends or during vacation, patients will sleep considerably longer
- D. Polysomnography not necessary: sleep latency < 10 minutes and sleep efficiency > 90%.

Hypersomnia and excessive daytime sleepiness: common after stroke

Poststroke hypersomnia can be found after subcortical (in particular caudate-putamen), thalamomesencephalic, upper pontine, medial pontomedullary, and even cortical strokes. In a recent study of 285 consecutive patients, we observed that at 21 ± 18 months after stroke, hypersomnia (27% of cases with sleep needs ≥ 10 hours/day), EDS (28% with Epworth Sleepiness Score ≥ 10), and fatigue (46% with fatigue severity scale ≥ 3) are frequent. Al-



Excessive daytime sleepiness is common in Parkinson's disease

Zurich patients



48% are sleepy (Epworth sleepiness scale ≥ 10)
57% suffer from fatigue (fatigue severity scale ≥ 4)

~ disease duration and severity

sleep attacks are common

Arnulf et al. *Neurology* 2000. Valko et al. *Eur J Neurol* 2010.

Sleep-wake disturbances in Alzheimer's disease

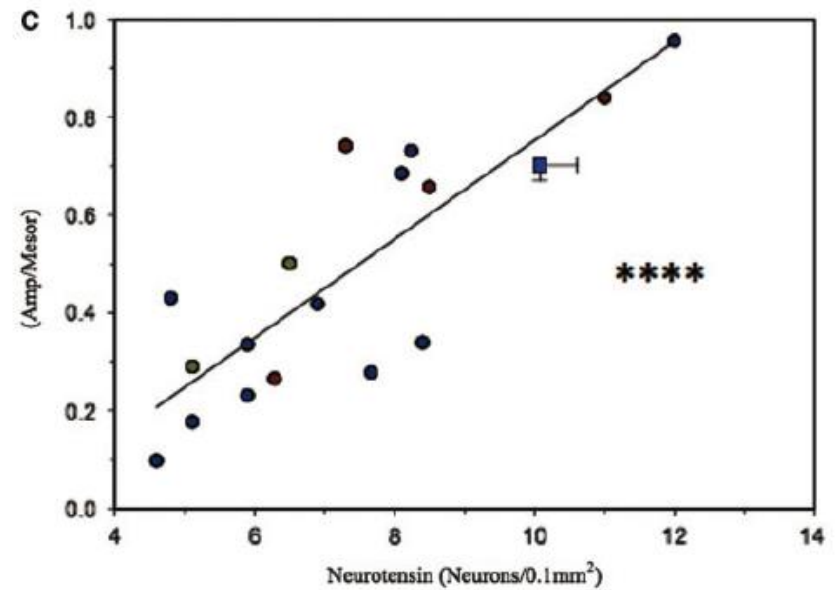
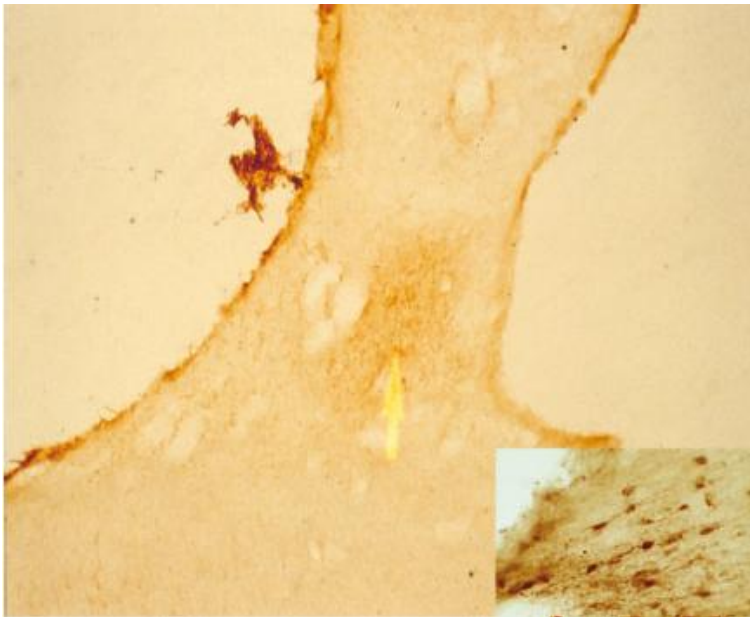
- Excessive daytime sleepiness
- Fatigue
- Fragmented nocturnal sleep
- Circadian sleep-wake disorders
- Confusional arousals

Excessive daytime sleepiness:

- Less frequent than in Parkinson's disease
- Associated with impaired cognitive function

Neurodegeneration in the suprachiasmatic nucleus in Alzheimer's disease

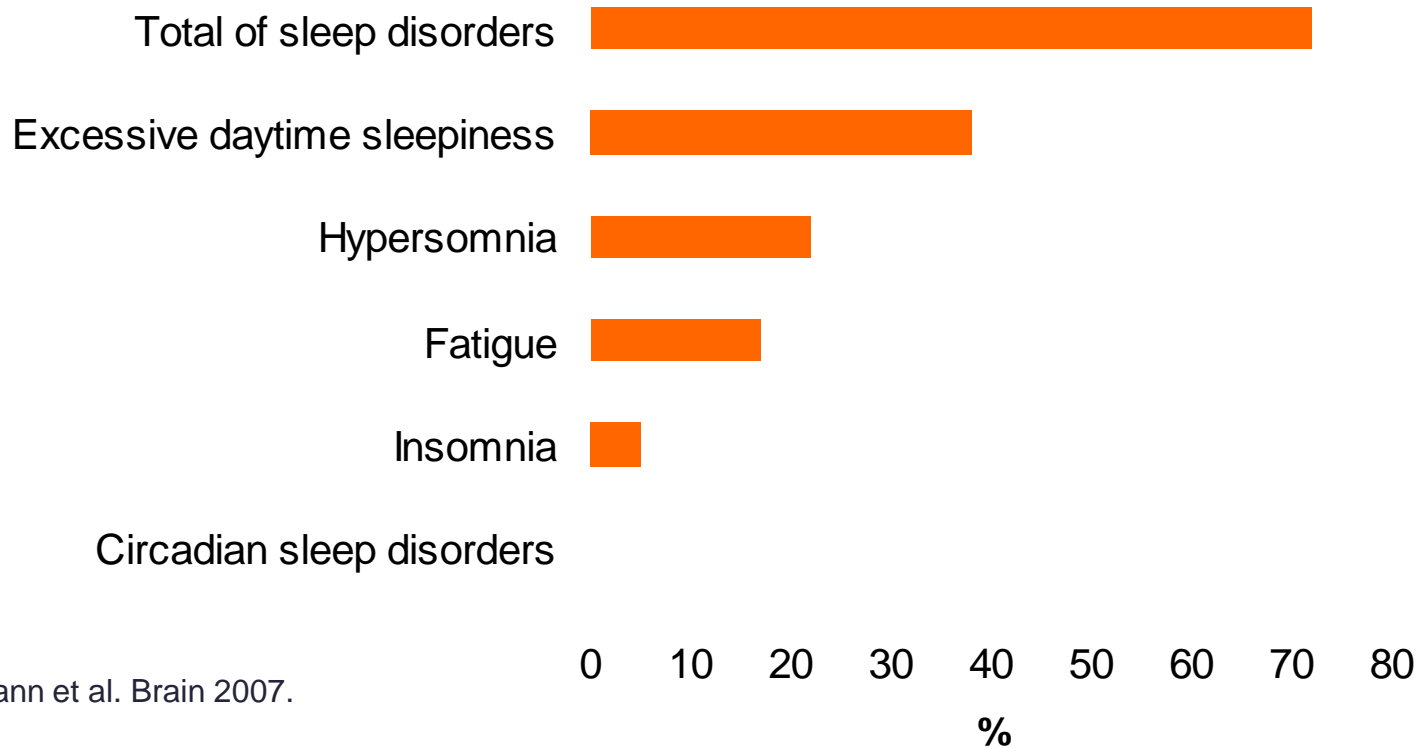
Loss of relative amplitude of activity reduced with reduction in neuronal density



Harper et al., Brain 2008.

Excessive daytime sleepiness and hypersomnia are common after Traumatic Brain injury

Prospective study of 65 consecutive patients with traumatic brain injury (TBI).

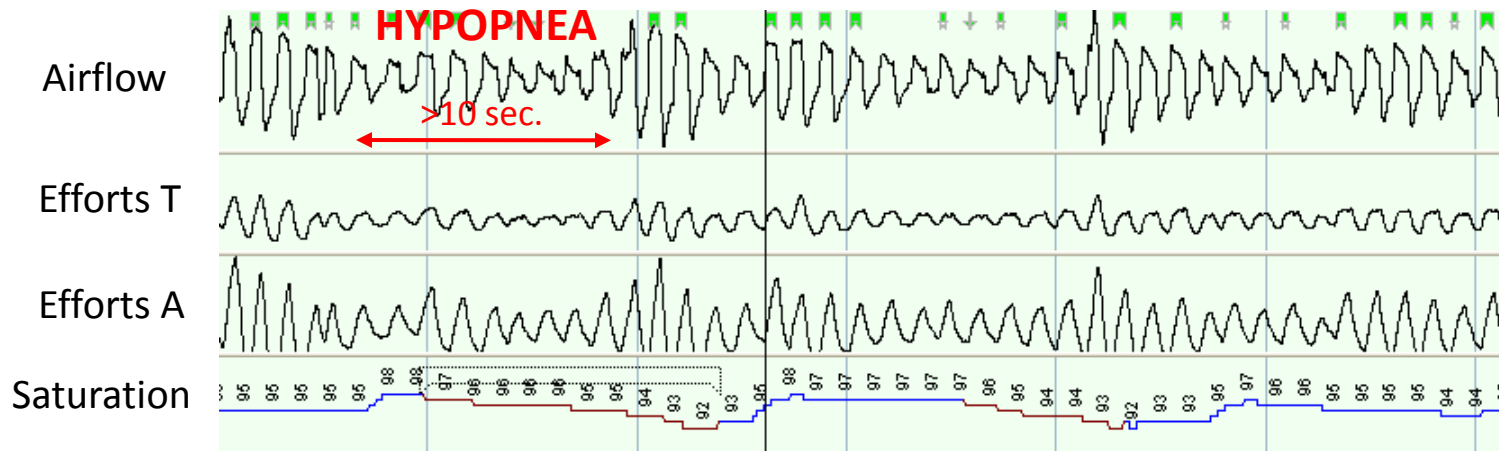
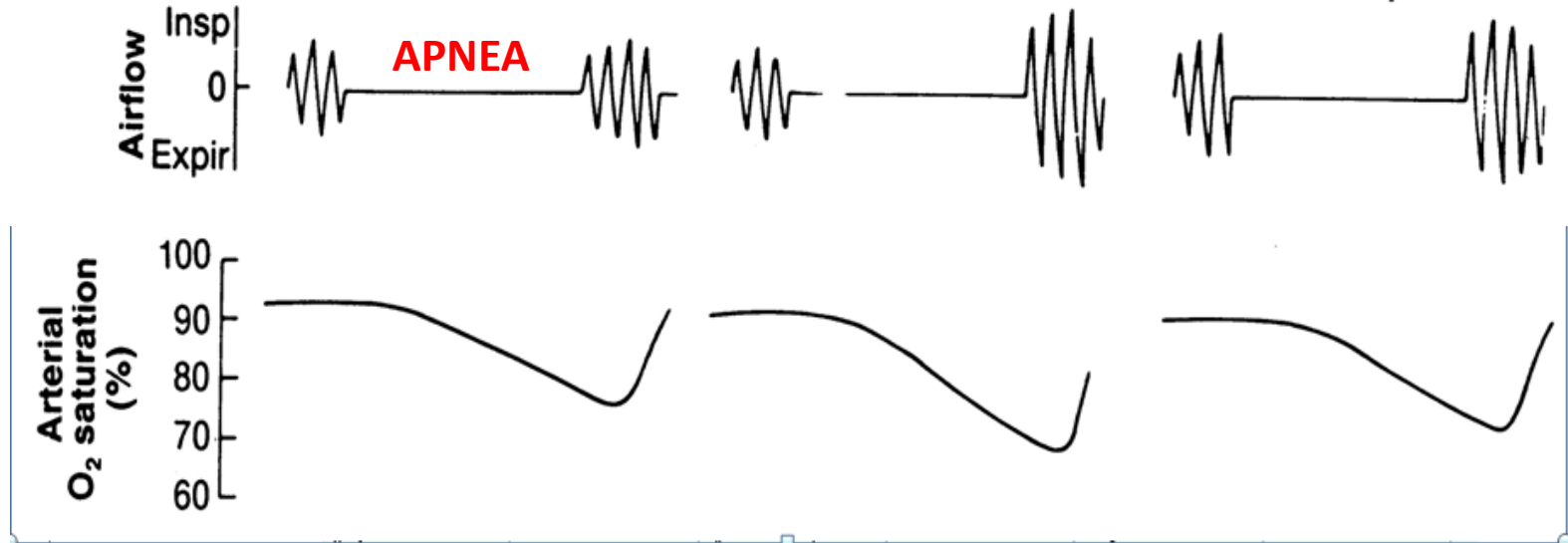


Baumann et al. Brain 2007.

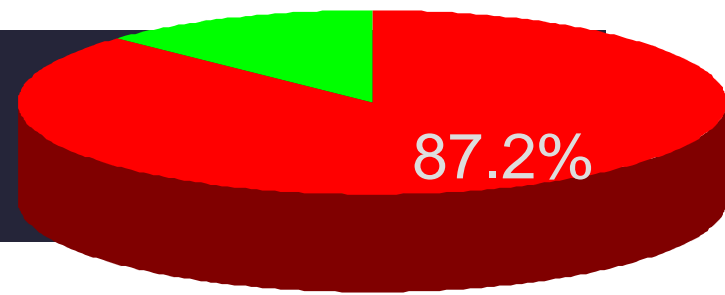
SLEEP-RELATED BREATHING DISORDERS

Obstructive Sleep Apnea

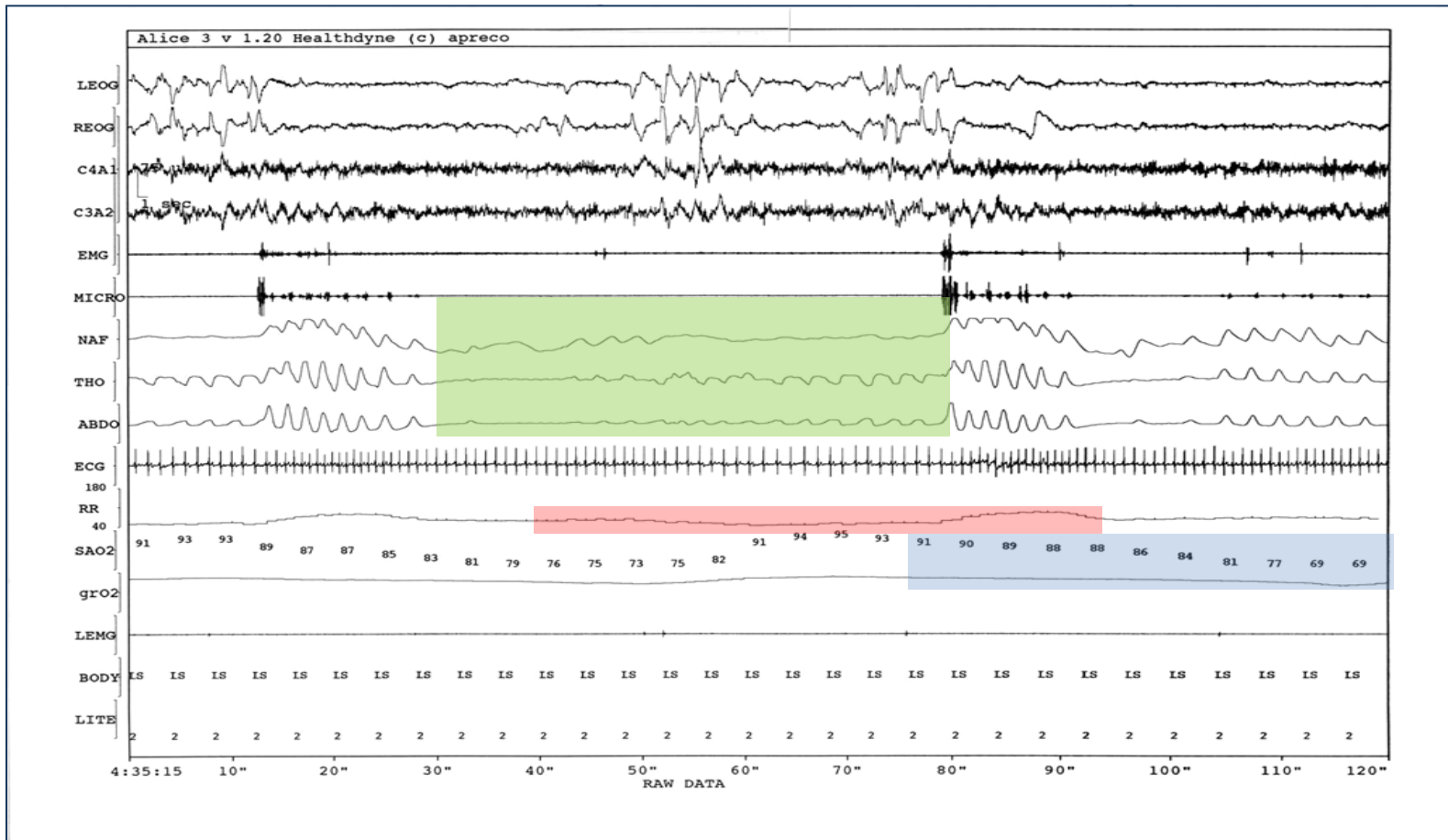
Examination: PSG:



Sleepiness: common in obstructive sleep apnea



Excessive daytime sleepiness in obstructive sleep apnea: prevalence, severity, and predictors[☆]



SLEEP-RELATED BREATHING DISORDERS

Obstructive Sleep Apnea

Symptoms:

- Excessive daytime sleepiness
- Loud snoring
- Episodes of breathing cessation during sleep witnessed by another person
- Abrupt awakenings accompanied by shortness of breath
- Awakening with a dry mouth or sore throat
- Morning headache
- Difficulty staying asleep (insomnia)
- Attention problems