

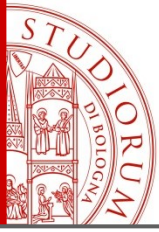
Physiological Regulations In Sleeping Mice

Stefano Bastianini

Department of Biomedical and Neuromotor Sciences (DIBINEM)

University of Bologna

e-mail stefano.bastianini3@unibo.it



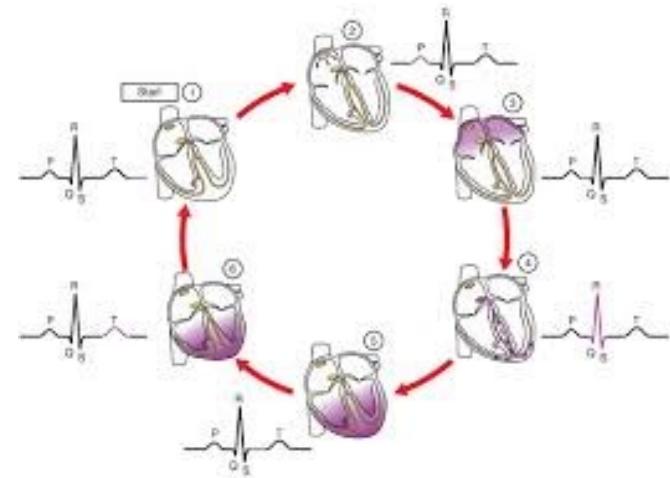
Scheme of this talk

- Electrical signals in animals
 - What is sleep and why do we care?
- Mice as models of physiology and pathology
 - Detection and analysis of physiological variables
 - Ongoing projects

Living systems can produce electricity

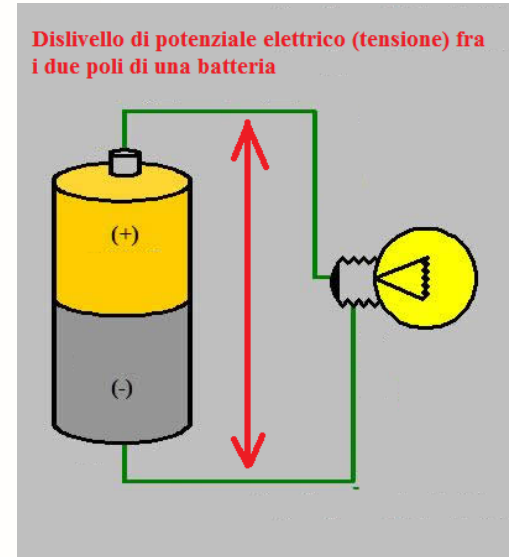
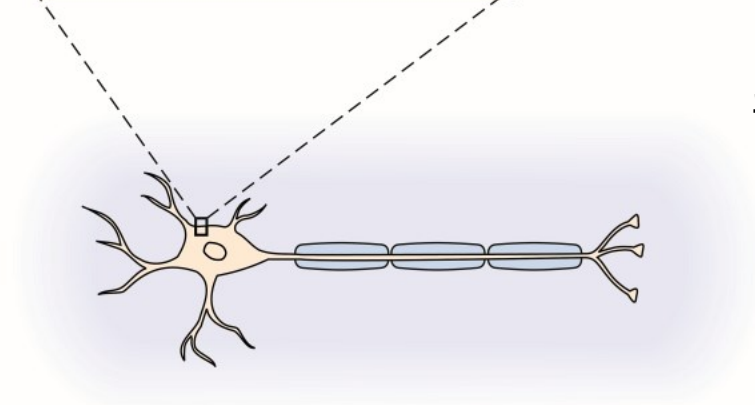
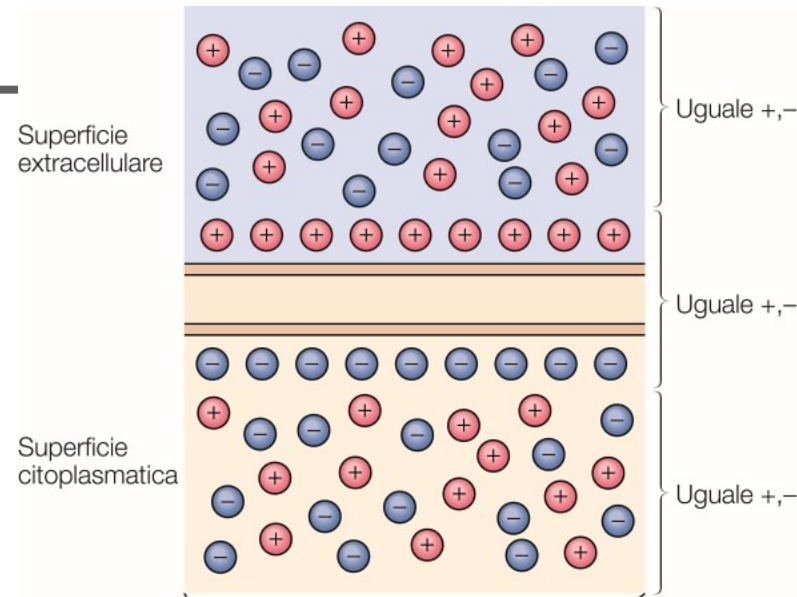


Neurons communicate with each other, forming the basis of our thoughts, behaviors, and perceptions.

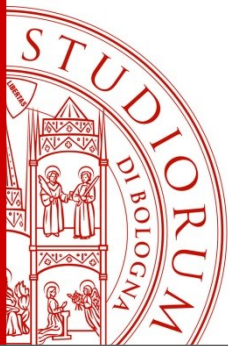


Muscle cells generate electrical signals before they contract

Across the cellular membrane there is an excess of negative charges inside the cell and positive charges outside of it

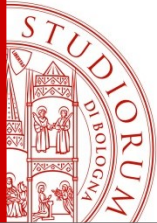


Just like a battery



Action Potential Propagation

© Sinauer Associates, Inc.



Scheme of this talk

- Electrical signals in animals
- What is sleep and why do we care?
- Mice as models of physiology and pathology
 - Detection and analysis of physiological variables
 - Ongoing projects

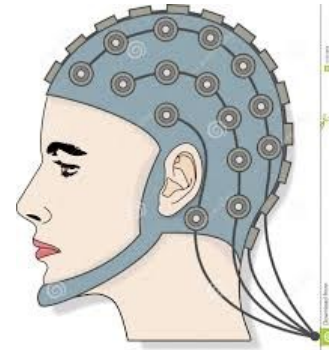
Sleep

- Sleep is one of the most important human behaviors, indeed it occupies about a third of our lives.
- The main characteristic is the reversible reduction of the response threshold to external stimuli
- It is a universal phenomenon found in all animals studied (from insects to mammals), therefore highly conserved in the evolutionary arc



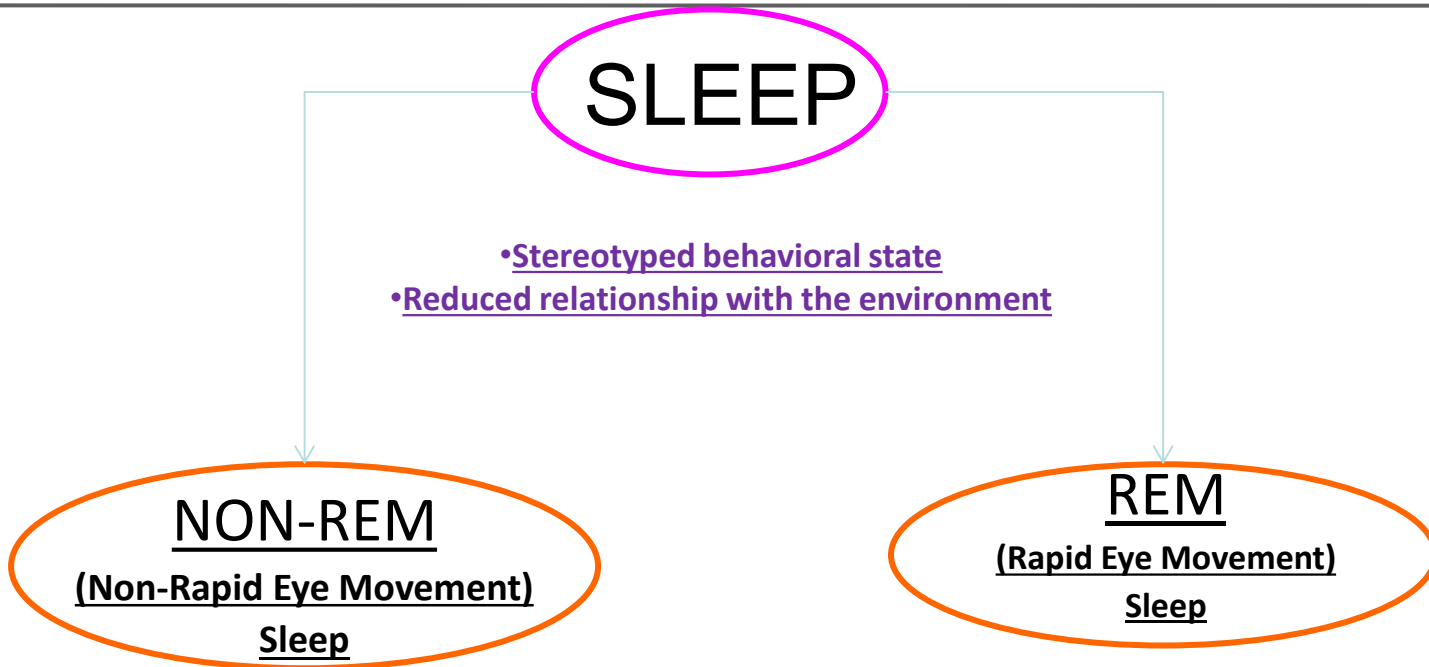


How can we study sleep behavior?



The electroencephalogram (EEG) is a tool that detects the electrical activity of the brain

Only through the use of EEG we can actually be sure that an individual is sleeping since brain activity changes significantly between wakefulness and sleep.



REM sleep is present only in mammals and some birds.

Neurons work differently between wakefulness and sleep



WAKEFULNESS

Neurons work differently between wakefulness and sleep



SLEEP

EEG rhythms

Wakefulness: fast and desynchronized rhythms

Slow Wave Sleep stage 1: light sleep

Slow Wave Sleep stage 2: synchronization of EEG

Rhythms:

- Alfa = 8-13 Hz (Eyes closed)
- Beta = 14-30 Hz (Wake)
- Sigma = 12-14 Hz (spindles)



Correlate with memory consolidation

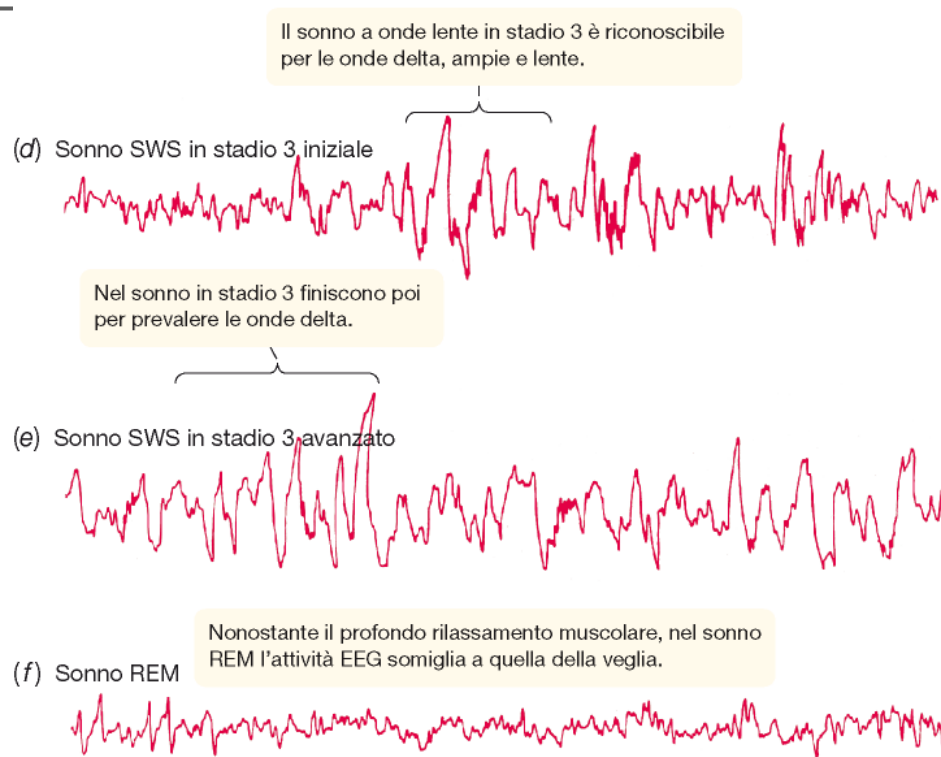
EEG rhythms

Slow Wave Sleep stage 3:
deep sleep, EEG highly
synchronized

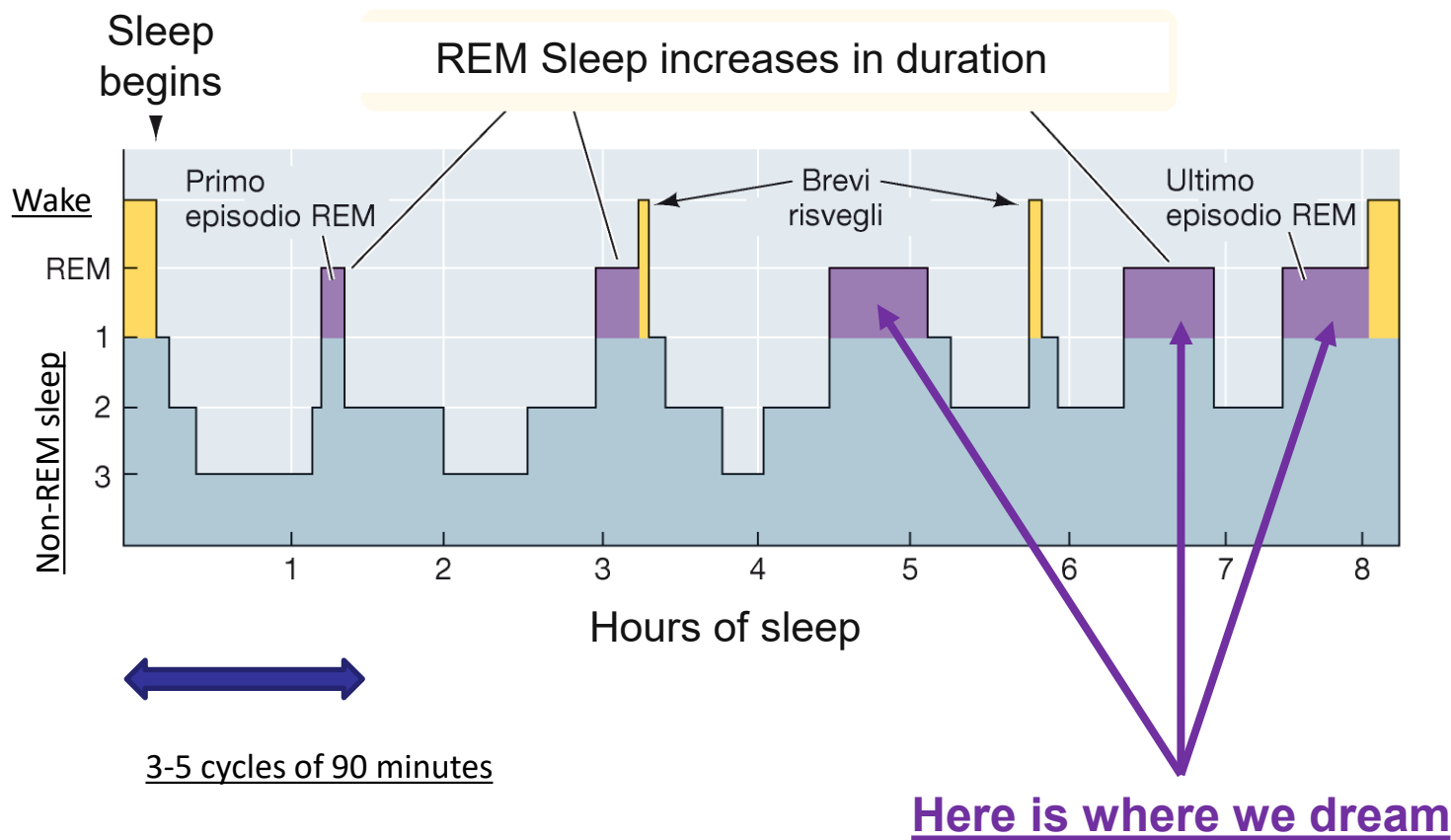
REM: fast and desynchronized
rhythms

Rhythms:

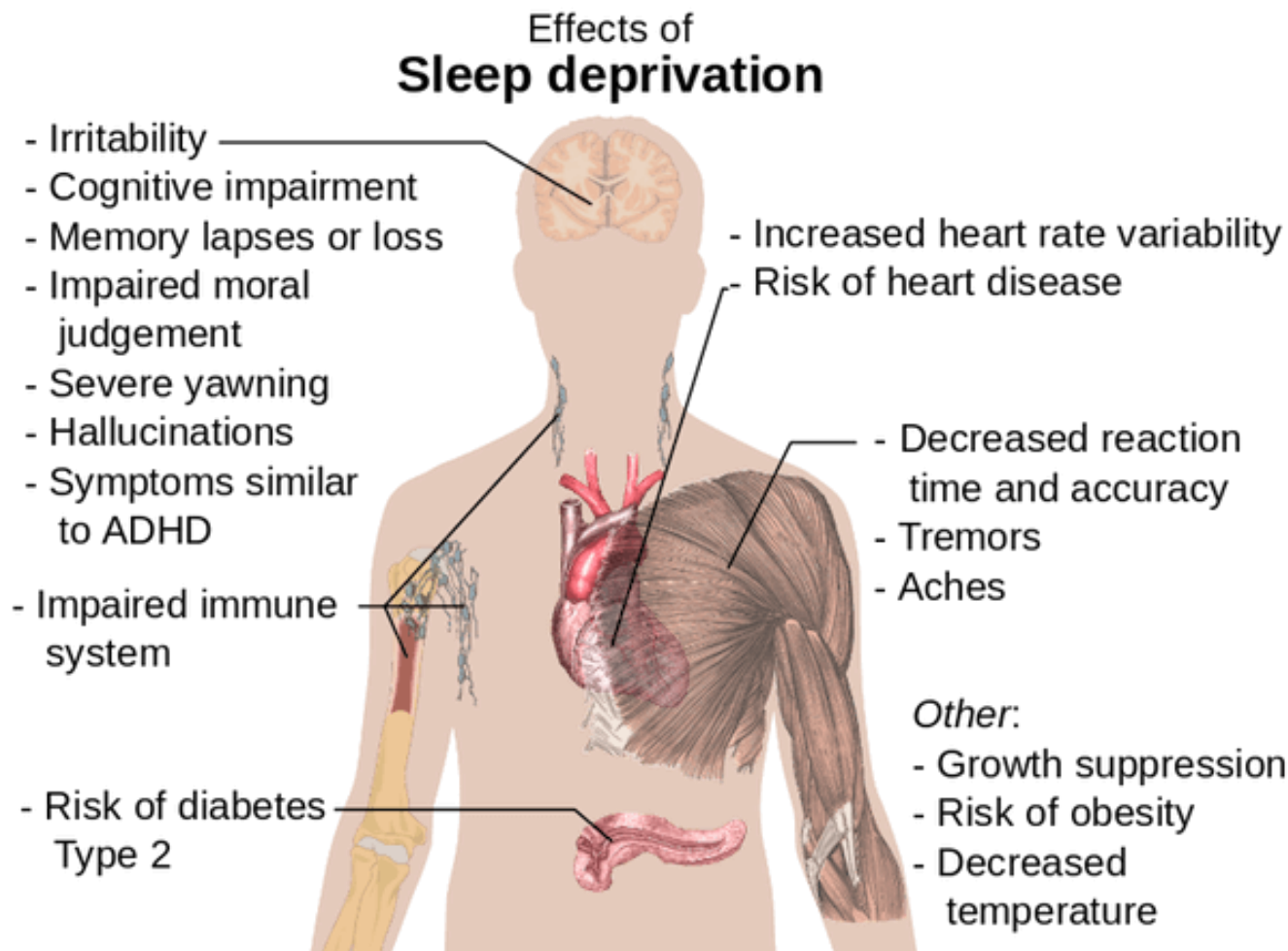
- Delta = 0,5-4 Hz (slow waves)
- Theta = 4-7,5 Hz (W and REM)

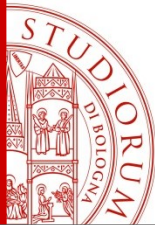


Hypnogram



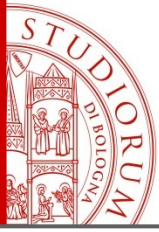
Why do we care about sleep?





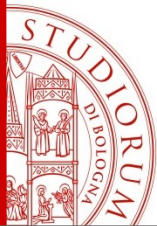
List of Sleep Problems

Insomnia.....	
Chronic Insomnia Disorder	
Short-Term Insomnia Disorder	
Other Insomnia Disorder	
ISOLATED SYMPTOMS AND NORMAL VARIANTS	
Excessive Time in Bed	
Short Sleeper	
Sleep Related Breathing Disorders	
OBSTRUCTIVE SLEEP APNEA DISORDERS	
Obstructive Sleep Apnea, Adult	
Obstructive Sleep Apnea, Pediatric	
CENTRAL SLEEP APNEA SYNDROMES	
Central Sleep Apnea with Cheyne-Stokes Breathing.....	
Central Apnea Due to a Medical Disorder without Cheyne-Stokes Breathing.....	
Central Sleep Apnea Due to High Altitude Periodic Breathing.....	
Central Sleep Apnea Due to a Medication or Substance.....	
Primary Central Sleep Apnea.....	
Primary Central Sleep Apnea of Infancy.....	
Primary Central Sleep Apnea of Prematurity	
Treatment-Emergent Central Sleep Apnea.....	
SLEEP RELATED HYPOVENTILATION DISORDERS	
Obesity Hypoventilation Syndrome.....	
Congenital Central Alveolar Hypoventilation Syndrome	
Late-Onset Central Hypoventilation with Hypothalamic Dysfunction.....	
Idiopathic Central Alveolar Hypoventilation.....	
Sleep Related Hypoventilation Due to a Medication or Substance.....	
Sleep Related Hypoventilation Due to a Medical Disorder	
SLEEP RELATED HYPOXEMIA DISORDER	
Sleep Related Hypoxemia	
Snoring.....	139
Catathrenia	141
Central Disorders of Hypersomnolence.....	
Narcolepsy Type 1	
Narcolepsy Type 2	
Idiopathic 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	
ISOLATED SYMPTOMS AND NORMAL VARIANTS	
Long Sleeper.....	
Circadian Rhythm Sleep-Wake Disorders	
Delayed Sleep-Wake Phase Disorder	
Advanced Sleep-Wake Phase Disorder.....	
Irregular Sleep-Wake Rhythm Disorder	
Non-24-Hour Sleep-Wake Rhythm Disorder.....	
Shift Work Disorder	
Jet Lag Disorder	
Circadian Sleep-Wake Disorder Not Otherwise Specified (NOS)	
Parasomnias	
NREM-RELATED PARASOMNIAS	
Disorders of Arousal (From NREM Sleep).....	
Confusional Arousals	
Sleepwalking	
Sleep Terrors.....	
Sleep Related Eating Disorder.....	
REM-RELATED PARASOMNIAS	
REM Sleep Behavior Disorder	
Recurrent Isolated Sleep Paralysis.....	
Parasomnia, unspecified	279
ISOLATED SYMPTOMS AND NORMAL VARIANTS	
Sleep Talking.....	279
Sleep Related Movement Disorders	281
Restless Legs Syndrome	282
Periodic Limb Movement Disorder.....	292
Sleep Related Leg Cramps.....	299
Sleep Related Bruxism	303
Sleep Related Rhythmic Movement Disorder	312
Benign Sleep Myoclonus of Infancy.....	317
Propriospinal Myoclonus at Sleep Onset.....	321
Sleep Related Movement Disorder Due to a Medical Disorder	325
Sleep Related Movement Disorder Due to a Medication or Substance.....	326
Sleep Related Movement Disorder, Unspecified	327
ISOLATED SYMPTOMS AND NORMAL VARIANTS	
Excessive Fragmentary Myoclonus	328
Hypnagogic Foot Tremor and Alternating Leg Muscle Activation.....	330
Sleep Starts (Hypnic Jerks)	335
Other Sleep Disorder.....	339
Appendix A:	
Sleep Related Medical and Neurological Disorders.....	341
Fatal Familial Insomnia	342
Sleep Related Epilepsy.....	345
Sleep Related Headaches	350
Sleep Related Laryngospasm.....	355
Sleep Related Gastroesophageal Reflux.....	358
Sleep Related Myocardial Ischemia.....	363
Appendix B:	
ICD-10-CM Coding for Substance-Induced Sleep Disorders.....	369



Scheme of this talk

- Electrical signals in animals
 - What is sleep and why do we care?
- Mice as models of physiology and pathology
 - Detection and analysis of physiological variables
 - Ongoing projects



The mouse is the species of choice for studies on functional genomics... and also on sleep



sleep mice



Search

[Advanced](#) [Create alert](#) [Create RSS](#)

[User Guide](#)

Save

Email

Send to

Sort by: Most recent



Display options

MY CUSTOM FILTERS

13,331 results



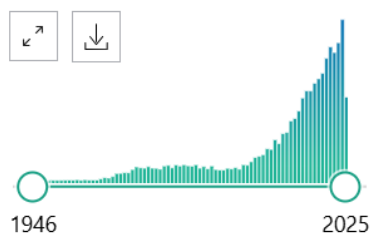
Page

1

of 1,334



RESULTS BY YEAR



1

Cite

Share

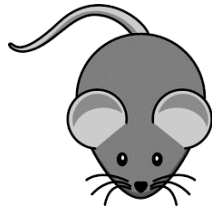
Lemon Verbena Extract Enhances **Sleep Quality and Duration via Modulation of Adenosine A1 and GABA(A) Receptors in Pentobarbital-Induced and Polysomnography-Based **Sleep** Models.**

Choi M, Koo YK, Kim N, Lee Y, Yim DJ, Kim S, Park E, Park SJ.

Int J Mol Sci. 2025 Jun 14;26(12):5723. doi: 10.3390/ijms26125723.

PMID: 40565187

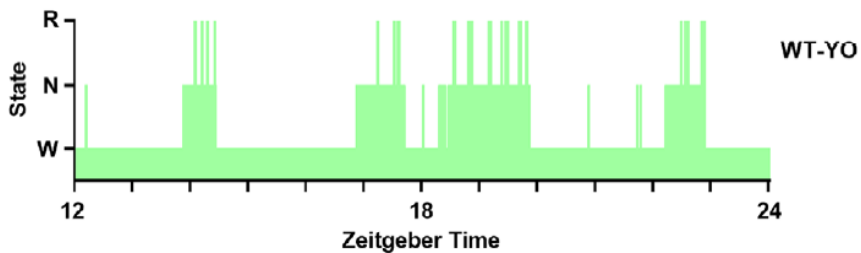
This study investigated the effects of lemon verbena extract (LVE) on **sleep** regulation using both a pentobarbital-induced **sleep** model and an EEG-based **sleep** assessment model in **mice**. ...Quantitative



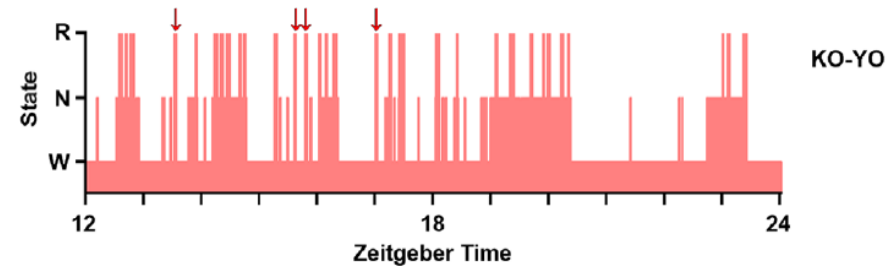
SLEEP IN RODENTS

Rodents: nocturnal animals
 polyphasic sleep
 fragmented wake-sleep cycle
 more NREM than humans
 NREM sleep not divided in stages

(d)



(e)



Just an example...



Wakefulness fragmentation

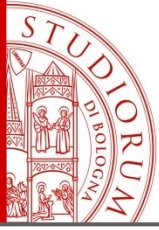
Reduced REMS latency

Cataplexy



Undetectable levels of brain Orexins

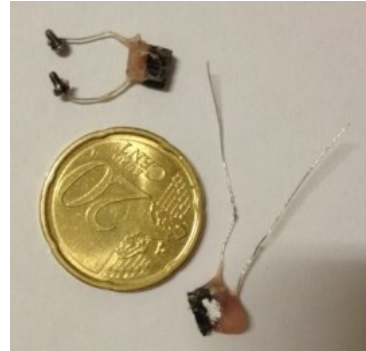
Narcoleptic phenotype



Scheme of this talk

- Electrical signals in animals
- What is sleep and why do we care?
- Mice as models of physiology and pathology
- Detection and analysis of physiological variables
- Ongoing projects

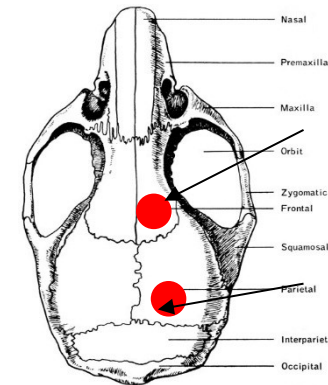
EEG/EMG minielectrodes



EEG: frontal-parietal, filterd 0.3–100 Hz

EMG: neck muscles, filterd 100–1000 Hz

Cable transmission; signals sampled at 1024 Hz



1 mm anterior
and 1 mm lateral
to bregma

1 mm anterior
and 1 mm lateral
to lambda

Blood pressure and heart rate telemetric transducer

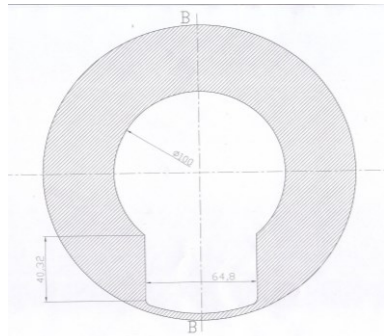
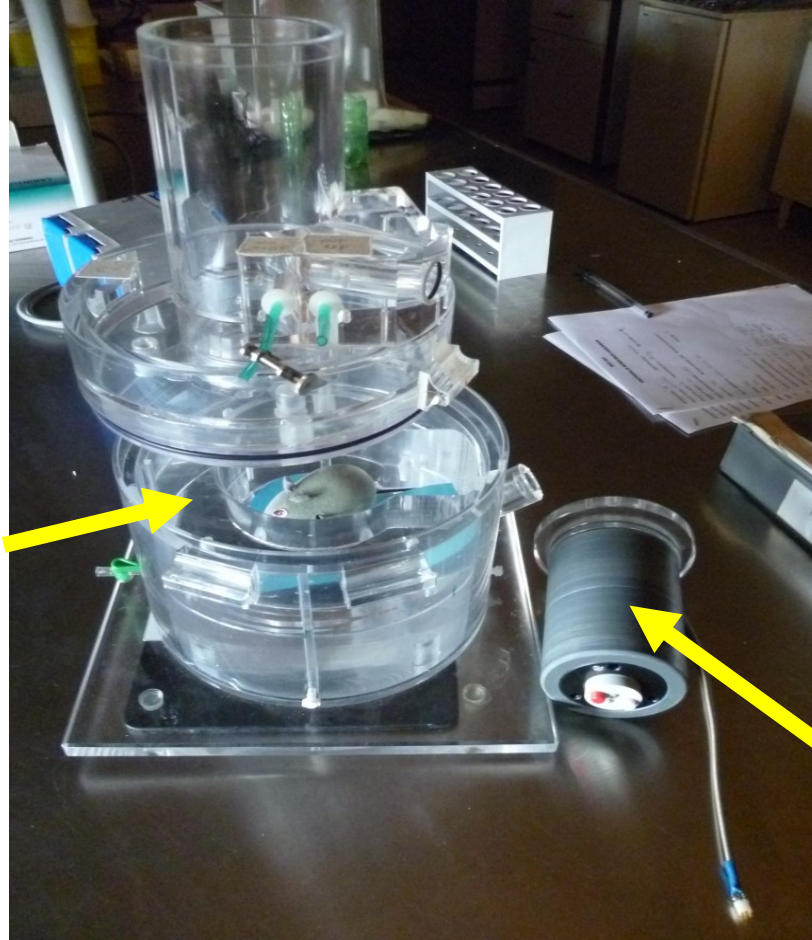
catheter insertion: femoral artery

catheter tip: abdominal aorta

transducer body: subcutaneous pouch on flank



Whole-body plethysmography



internal plexiglas chamber

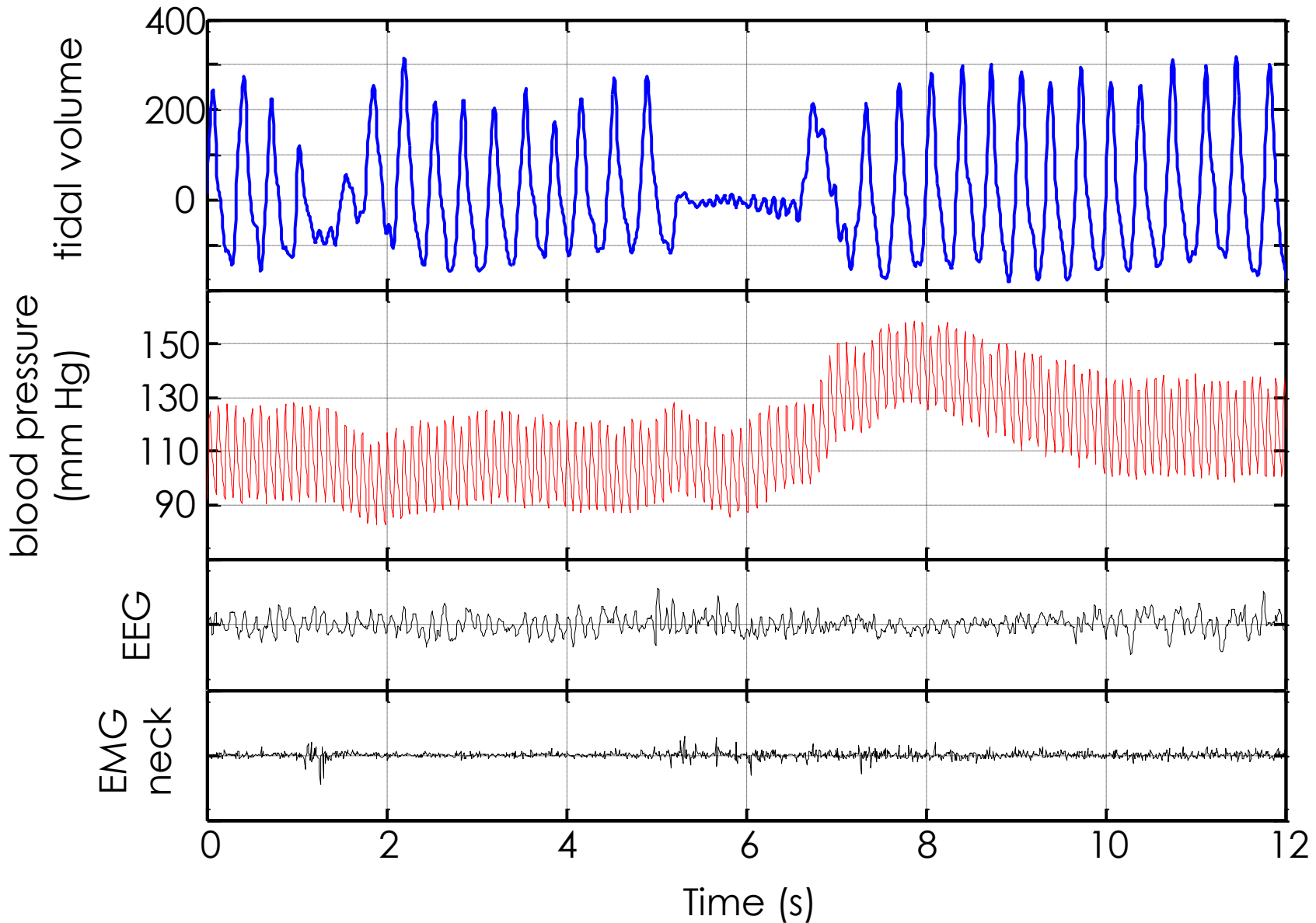


high-sensitivity differential pressure transducer

plastics plug with electrical swivel

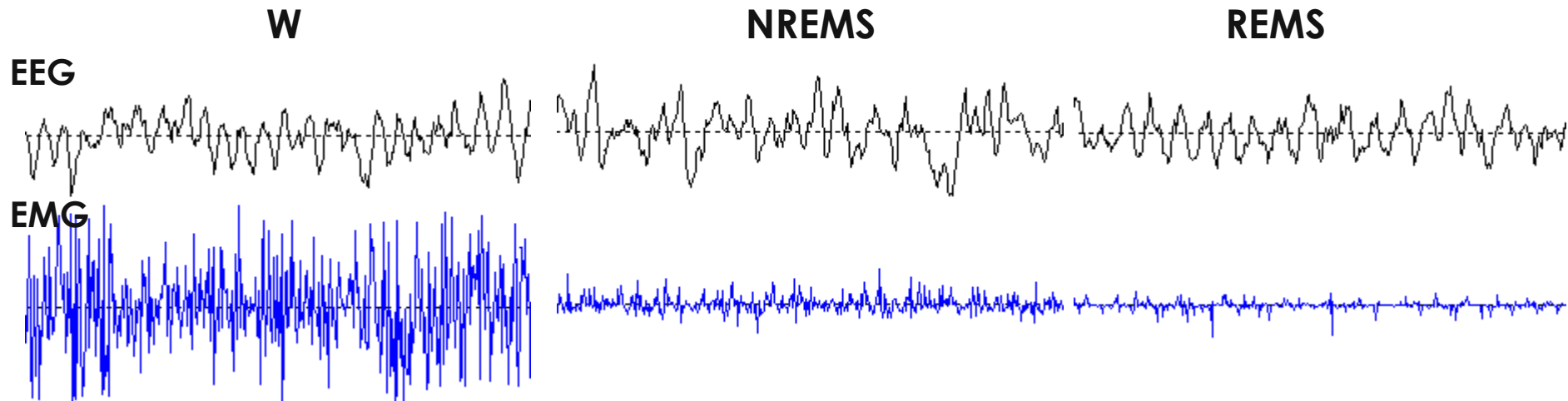
modified whole-body plethysmograph

Simultaneous measurement of breathing and blood pressure

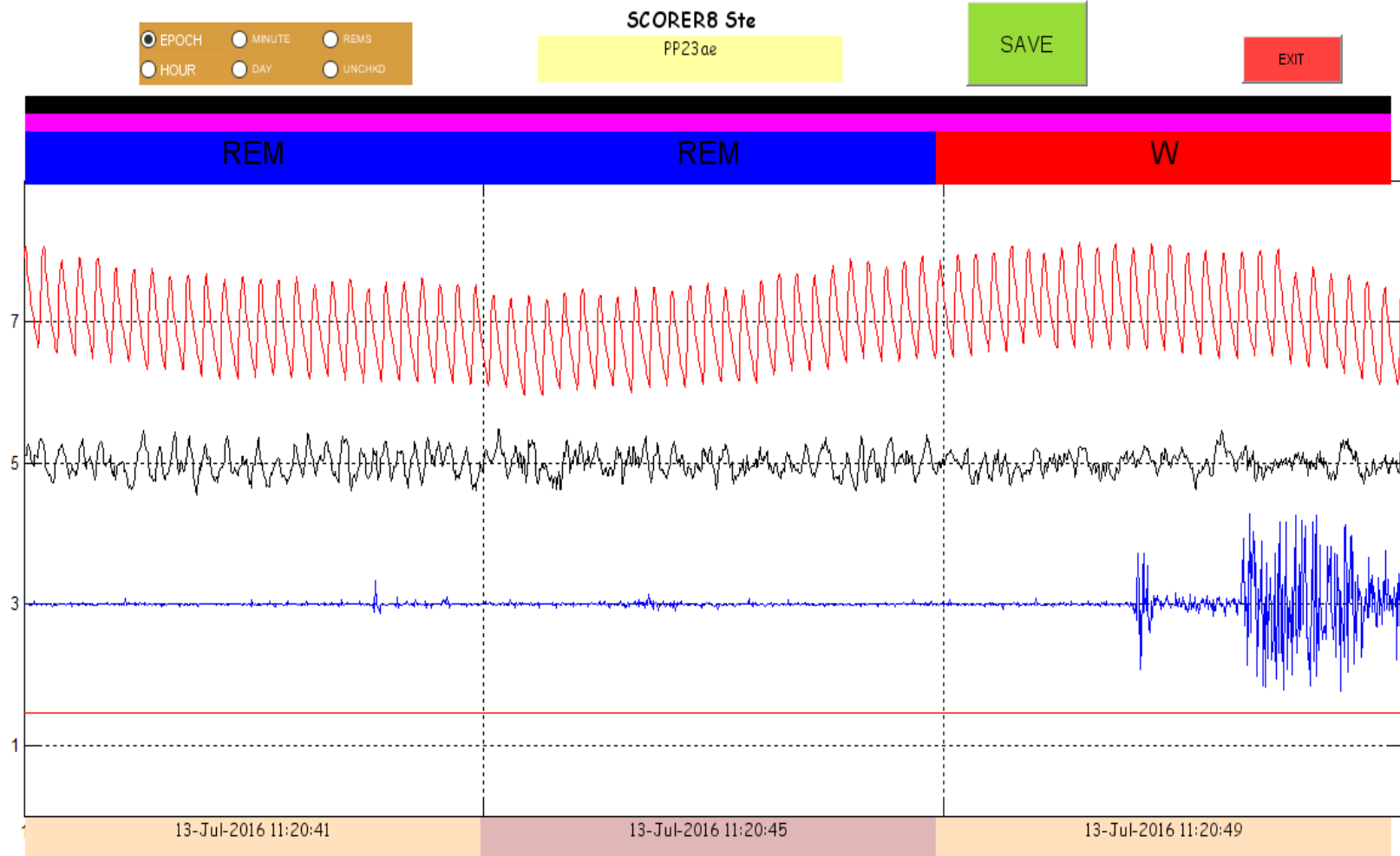


Scoring performed on 4 s epochs, based on EEG/EMG signals

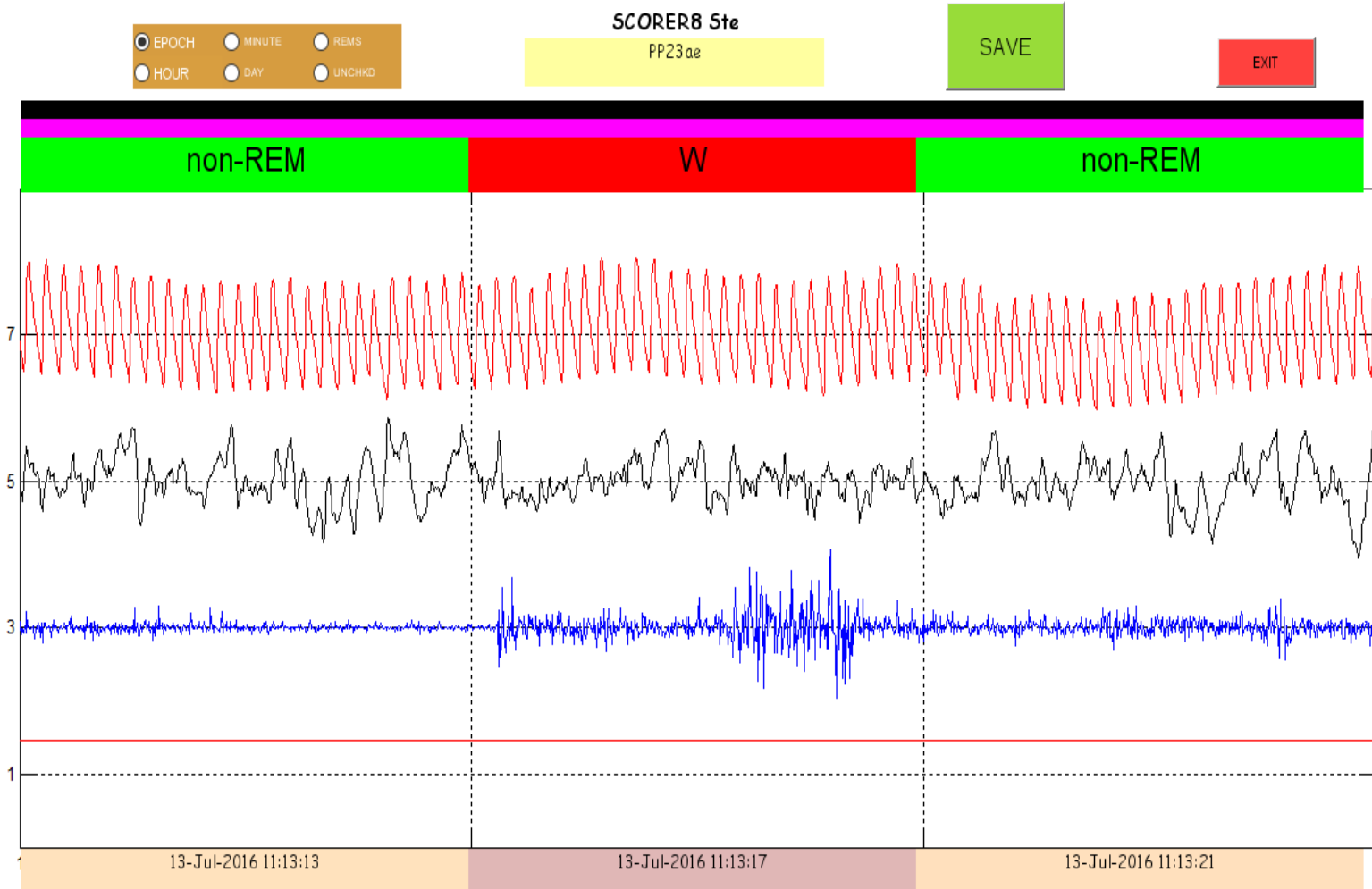
- W: EMG: high tone
 EEG: low voltage, possible θ (6–9 Hz) components
- NREMS: EMG lower than in W
 EEG: high voltage, prominent δ (0.5–4 Hz) components
- REMS: EMG muscle atonia, occasional muscle twitches
 EEG: low voltage, predominant θ components



SCORING SLEEP/AROUSALS IN RODENTS



SCORING SLEEP/AROUSALS IN RODENTS



Power spectrum analysis of EEG to highlight wake-sleep cycle differences

knockout, WT, wild type, YO, young.

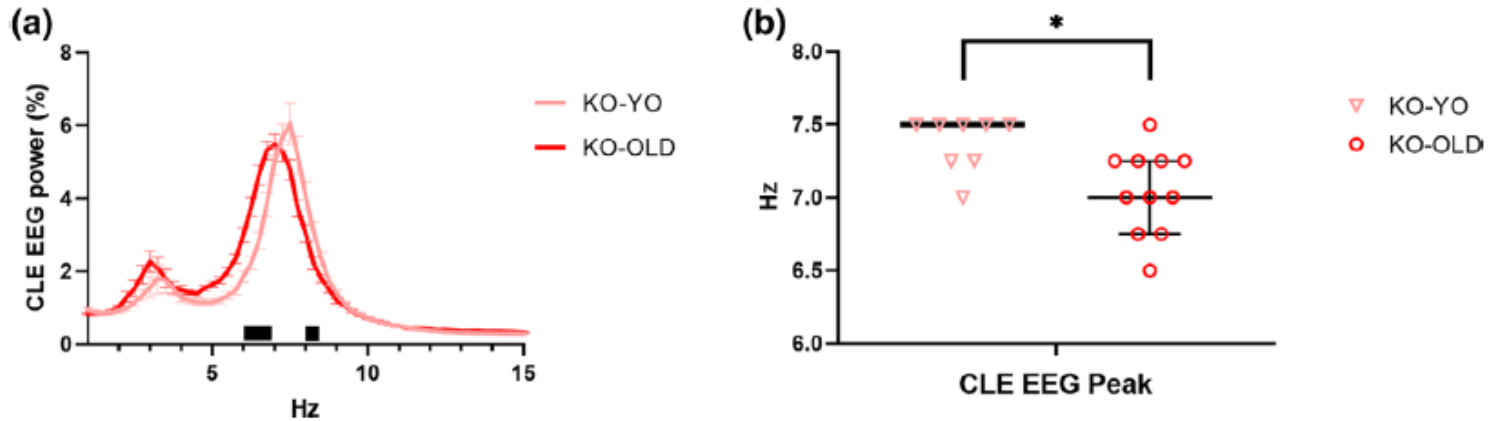
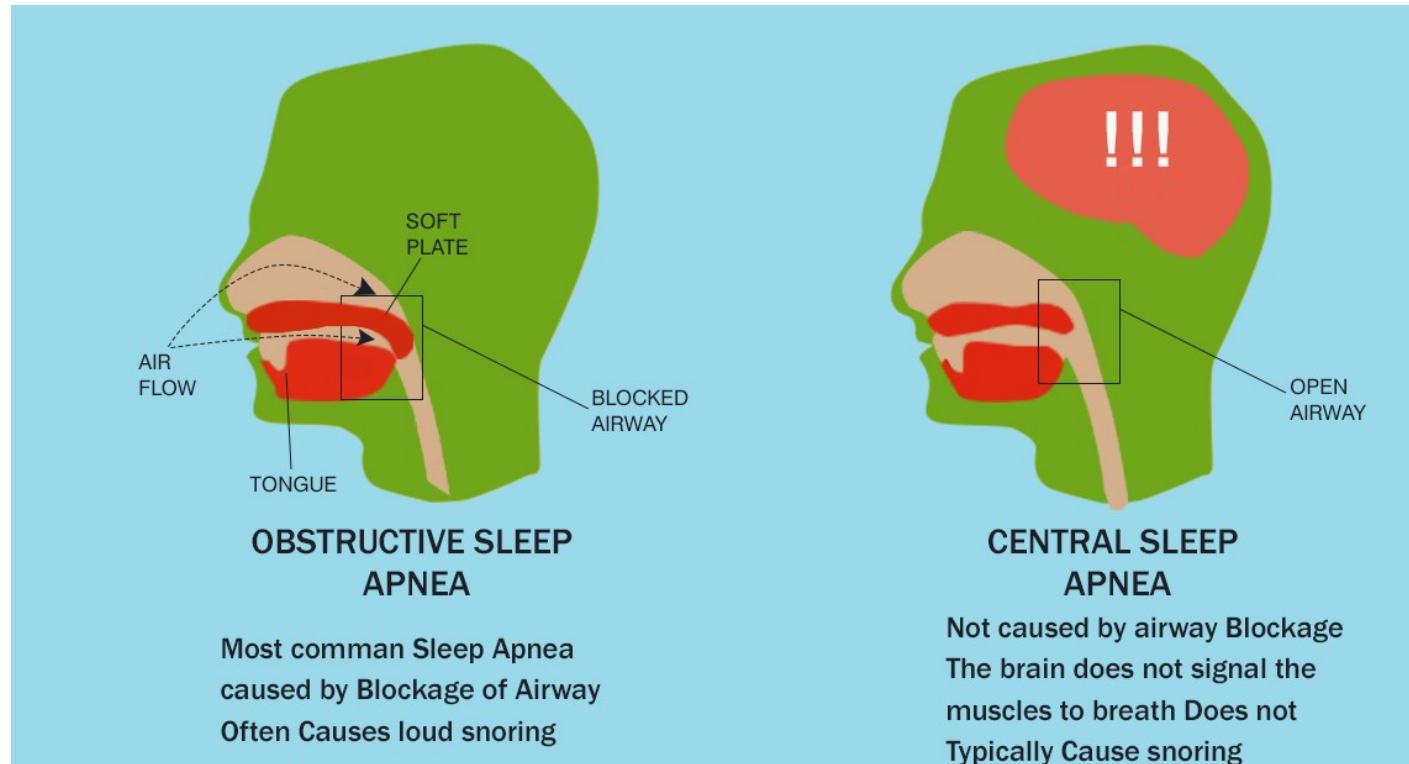
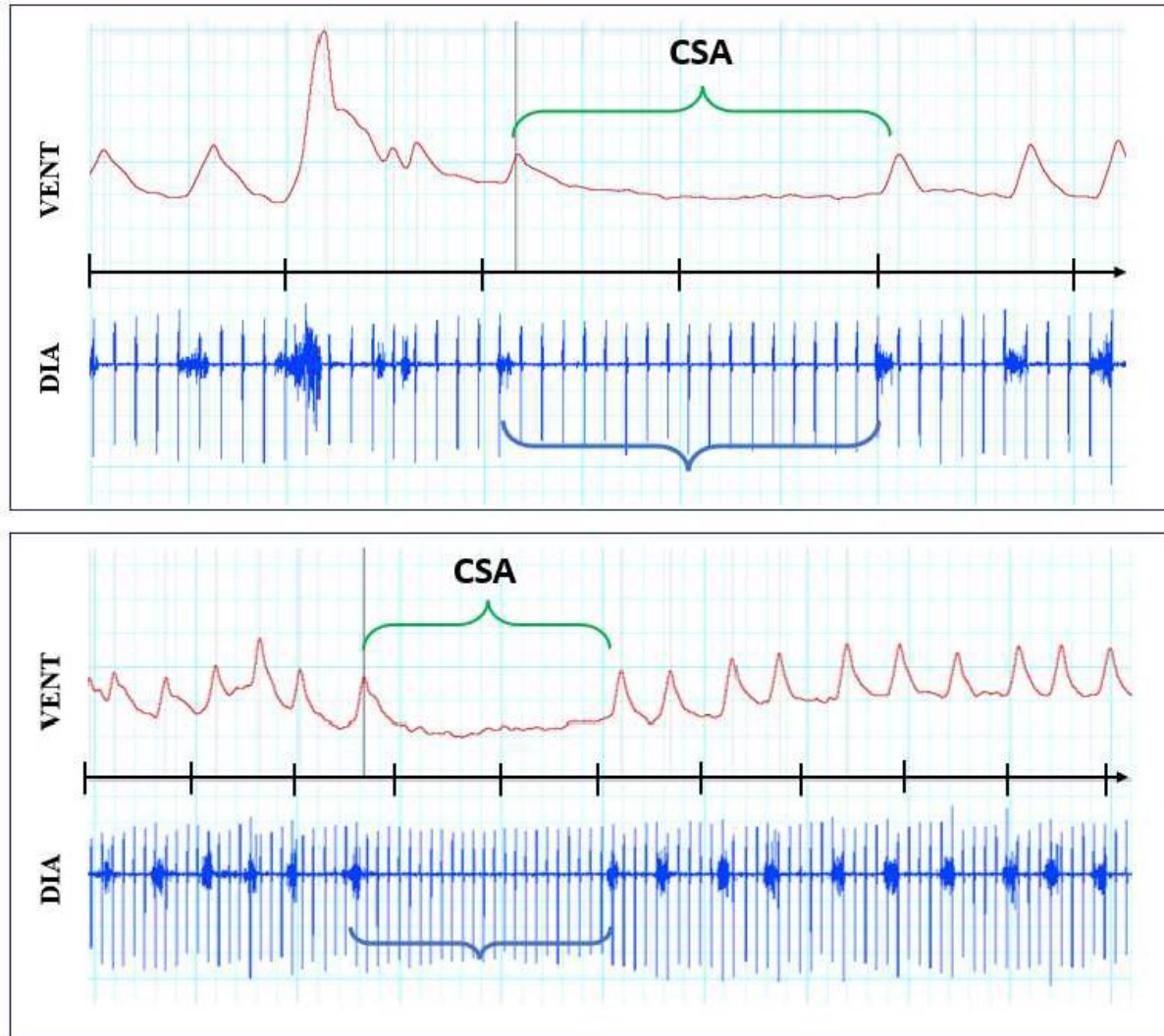


FIGURE 4 Electroencephalogram spectral analysis during cataplexy-like episodes. Electroencephalographic (EEG) spectral power (expressed as mean $\pm$ SEM of the percentage of total EEG spectral power) and peak (median with the 95% confidence interval) during cataplexy-like episodes (CLE) are shown for OLD and young (YO) orexin-knockout (KO). * $p < 0.05$ for Mann-Whitney test with the false discovery rate correction, with significant Kruskal-Wallis test. Black bars indicate $p < 0.05$ for the post-hoc corrected comparison between KO-OLD and KO-YO mice with significant age $\times$ EEG frequency interaction.

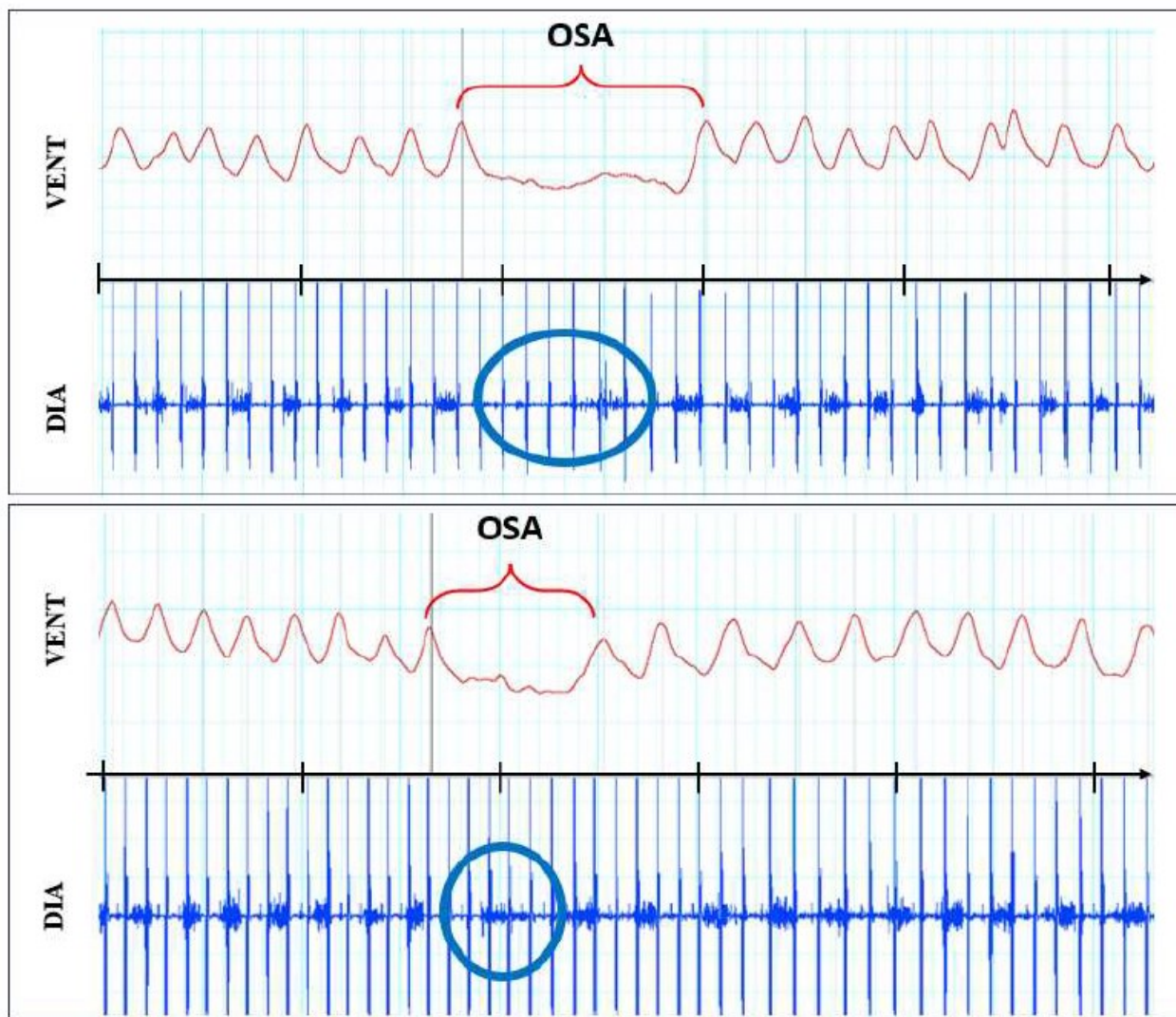
Central vs obstructive apnea during sleep

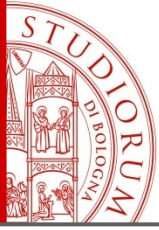


Central vs obstructive apnea during sleep



Central vs obstructive apnea during sleep





Scheme of this talk

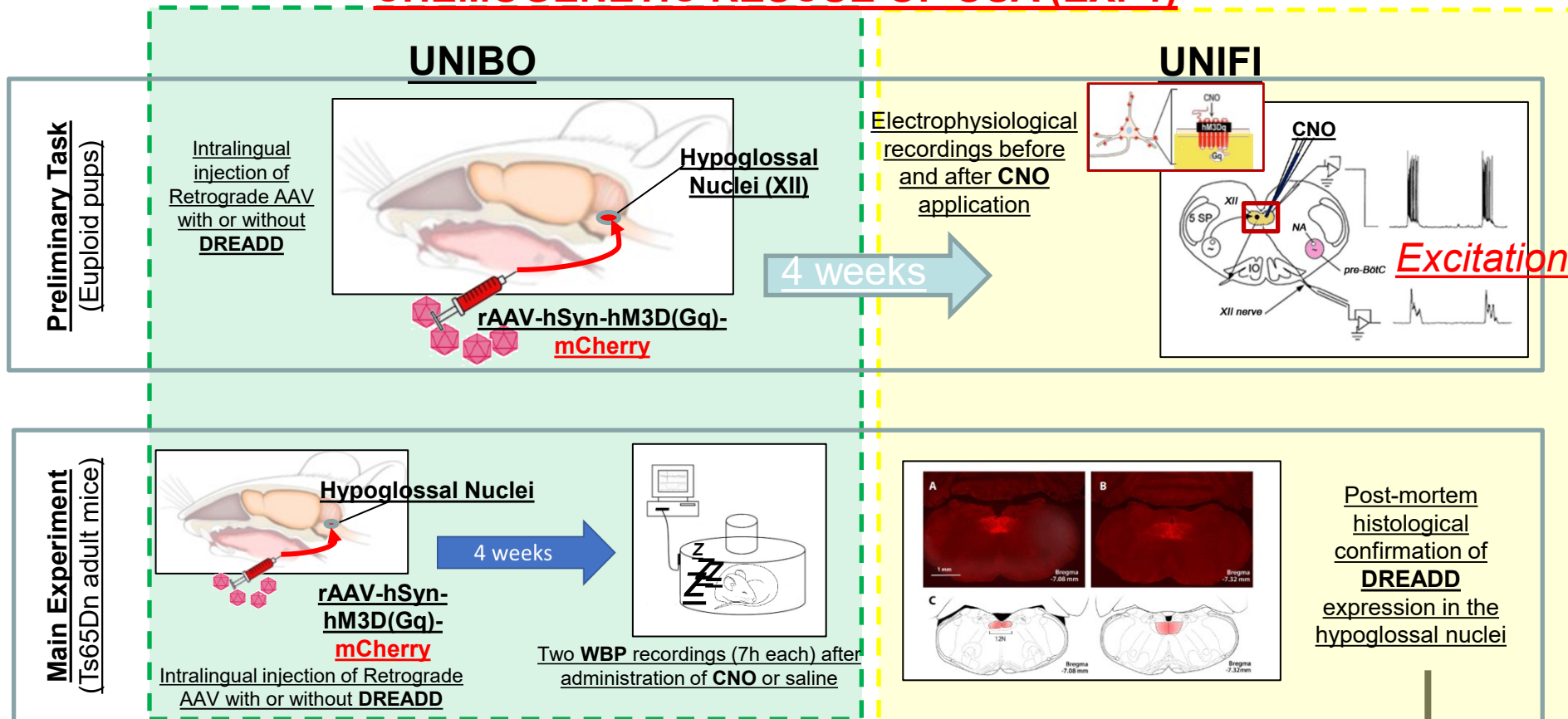
- Electrical signals in animals
 - What is sleep and why do we care?
- Mice as models of physiology and pathology
 - Detection and analysis of physiological variables
- Ongoing projects

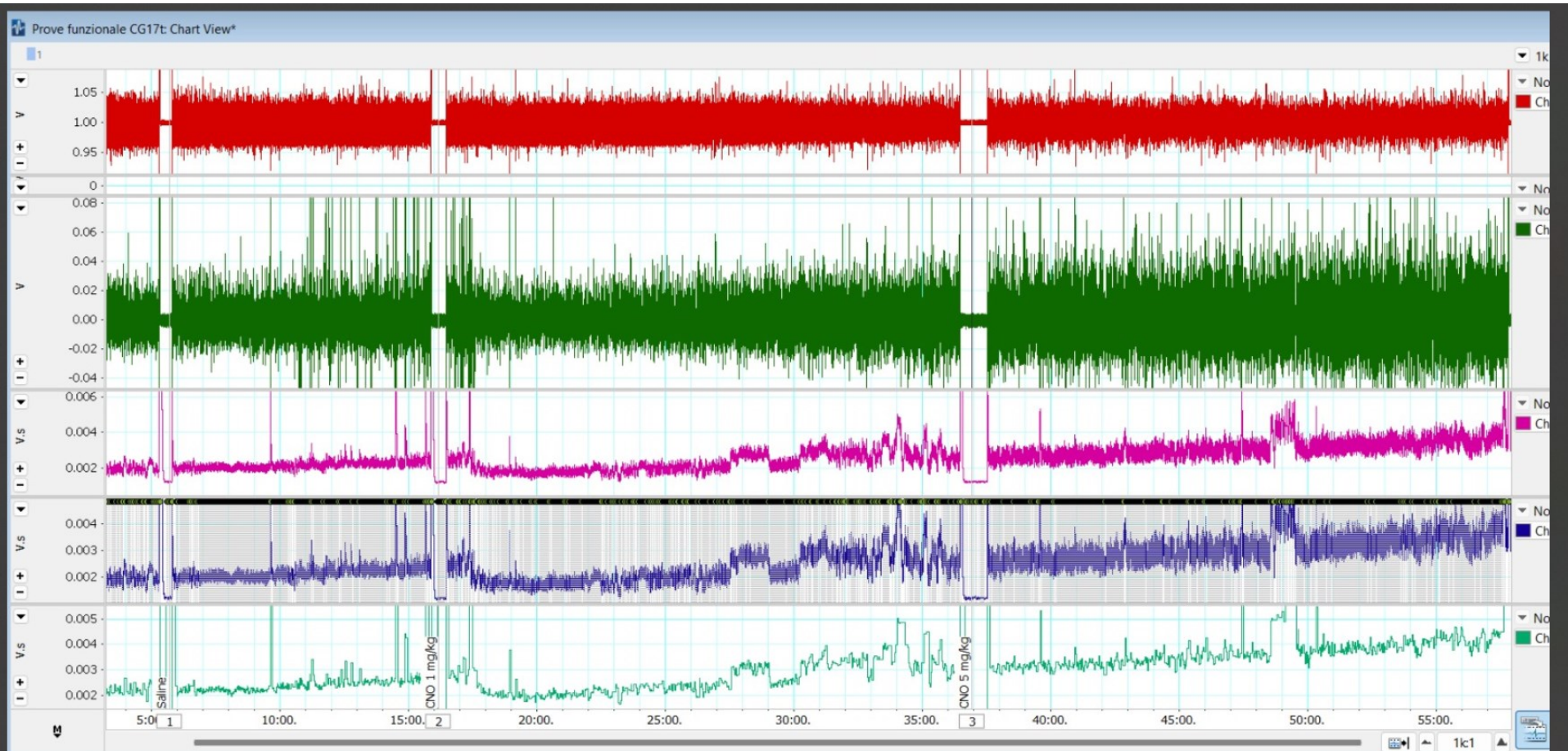
PART A

1. Research project title

Chemogenetic and Optgenetic Rescue of Sleep Apnea (COSA) in mice

CHEMOGENETIC RESCUE OF OSA (EXP1)





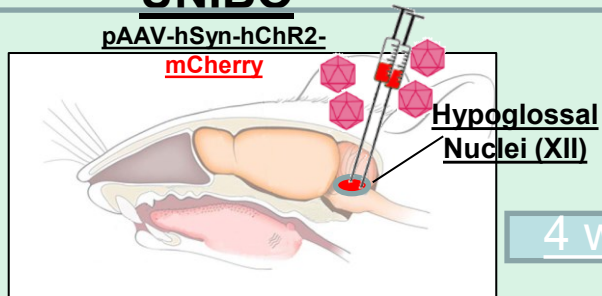
OPTOGENETIC RESCUE OF OSA (EXP2)

Preliminary Task (Euploid pups)

Brainstem injections of AAV with or without **light-sensitive receptors**

UNIBO

pAAV-hSyn-hChR2-
mCherry

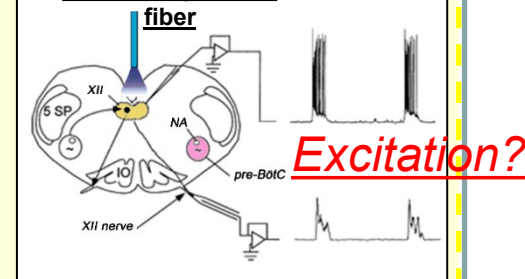


4 weeks

Electrophysiological recordings during different stimulating frequencies and pulse durations

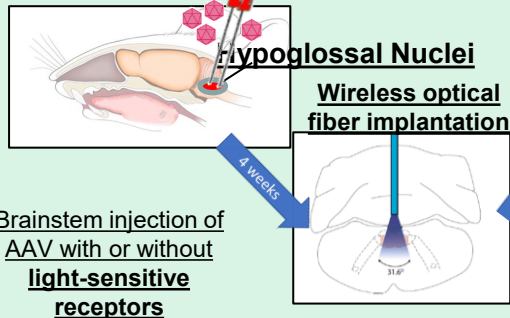
UNIFI

Stimulating optical

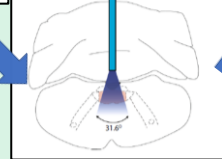


Main Experiment (Ts65Dn adult mice)

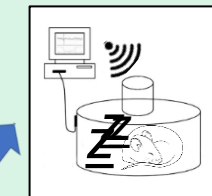
pAAV-hSyn-hChR2-
mCherry



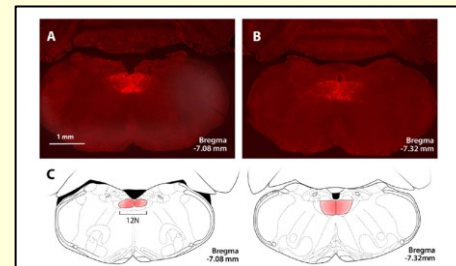
4 weeks



1 week

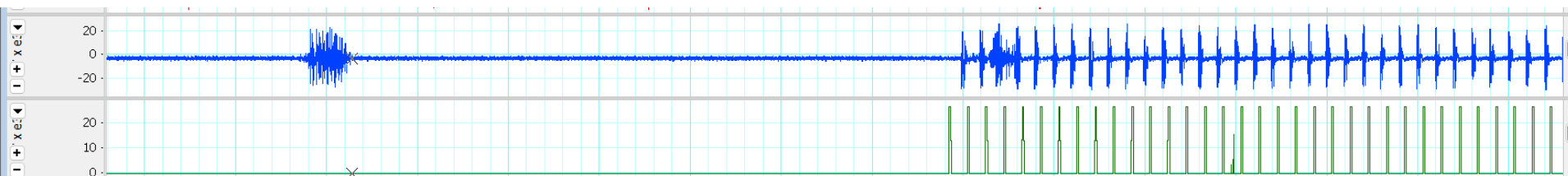


Two **WBP** recordings (7h each) with or without light stimulation during REM sleep

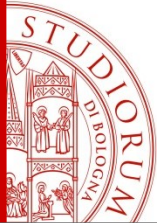


Post-mortem histological confirmation of **light-sensitive receptors** in the hypoglossal nuclei

Tongue EMG



Optical Stimulation



PRIN: PROGETTI DI RICERCA DI RILEVANTE INTERESSE NAZIONALE – Bando 2022 PNRR Prot. P2022RTCCA

PART A

1. Line of intervention

Main line/Linea Principale

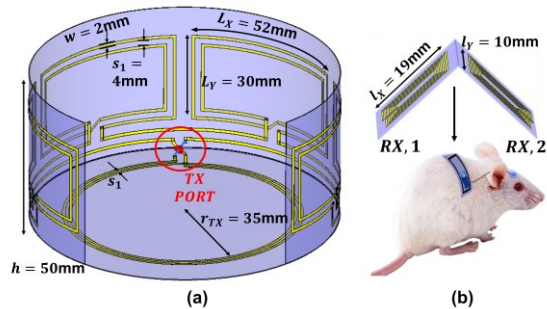
2. Research project title

ESTROSA: Energy-autonomous System for TRreatment of Obstructive Sleep Apnea

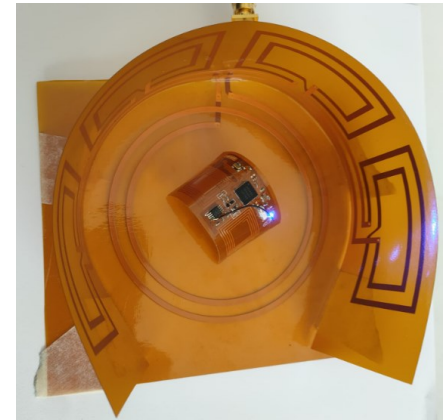
Methods

- To develop a WPT opto-stimulating system, we performed in-silico conceptualization, simulation and validation of transmitting and implantable receiving components. The design and optimization of these devices guarantees to harvest a minimum DC (Direct Current) power of 30 mW regardless of the position of the mouse inside the WBP chamber, to allow brain optogenetic stimulation using an implantable light-emitting diode (μ -ILED) directly controlled by a microcontroller unit.

Results



Schematic representation of the WPT system (left) and images of the prototype (right)



We designed and validated a transmitting multi-coil array operating at 13.56 MHz to be integrated into the walls of a circular mouse cage or WBP chamber. A pair of receiving coils with minimal size and weight were designed and validated to be implanted subcutaneously on the mouse back, together with the electronic circuitry for RF-to-DC power conversion and digital wireless control, then connected subcutaneously to a μ -ILED probe in the HN.

The in-silico validation of the proposed WPT opto-stimulating system was successful, supporting the achievement of a continuous power of ≥ 30 mW, independently of the position and orientation of the mouse inside the cage. This amount of harvested energy is sufficient for the wireless control of the implantable receiving device and to switch the μ -ILED on



Physiological Regulations In Sleeping Mice

Stefano Bastianini

Department of Biomedical and Neuromotor Sciences (DIBINEM)

University of Bologna

e-mail stefano.bastianini3@unibo.it