

Sleep in Pregnancy

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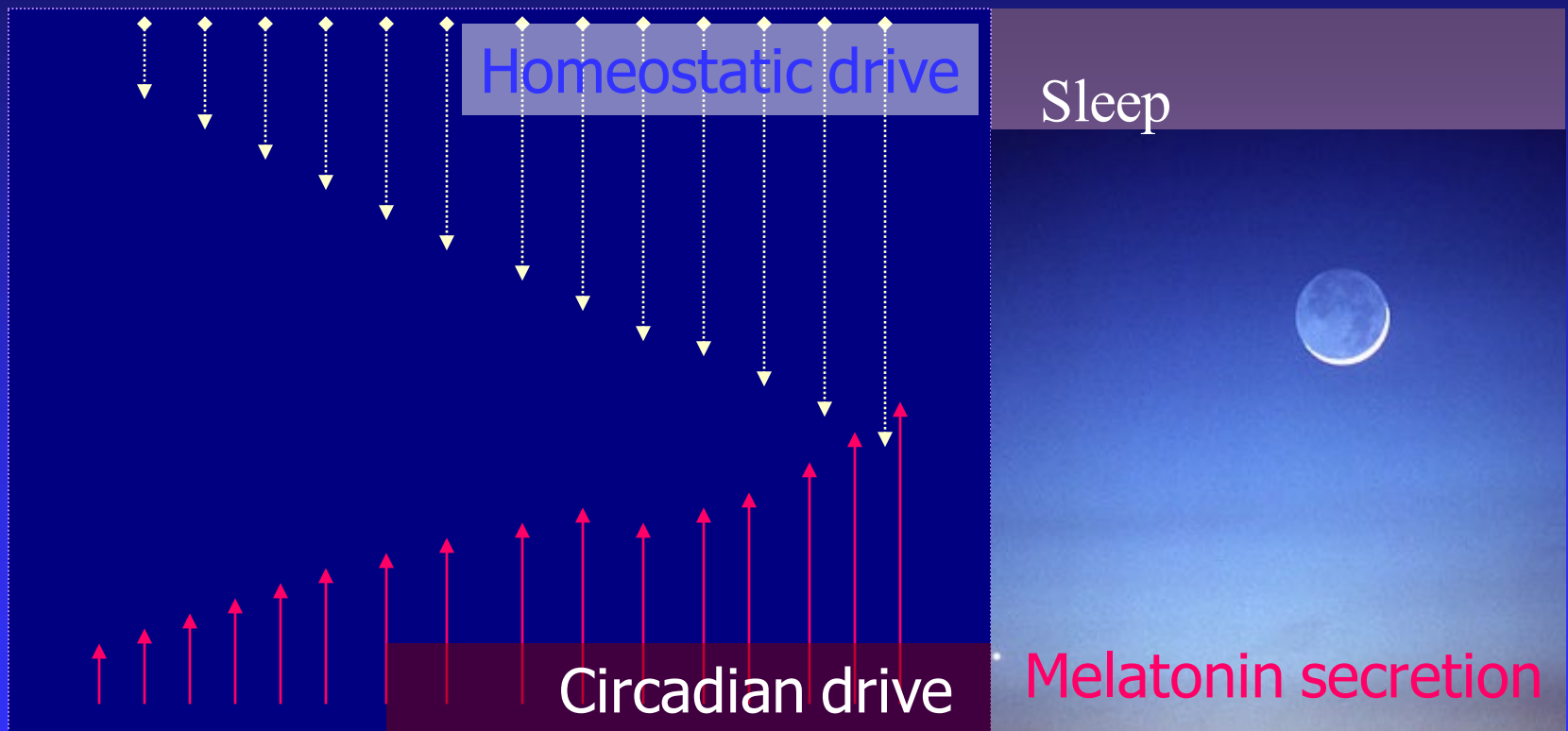
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Agenda

- Sleep physiology – introduction
- Causes of sleep disruption during pregnancy
- RLS/PLMD
- Insomnia
- Apnea (OSA vs. CSA)



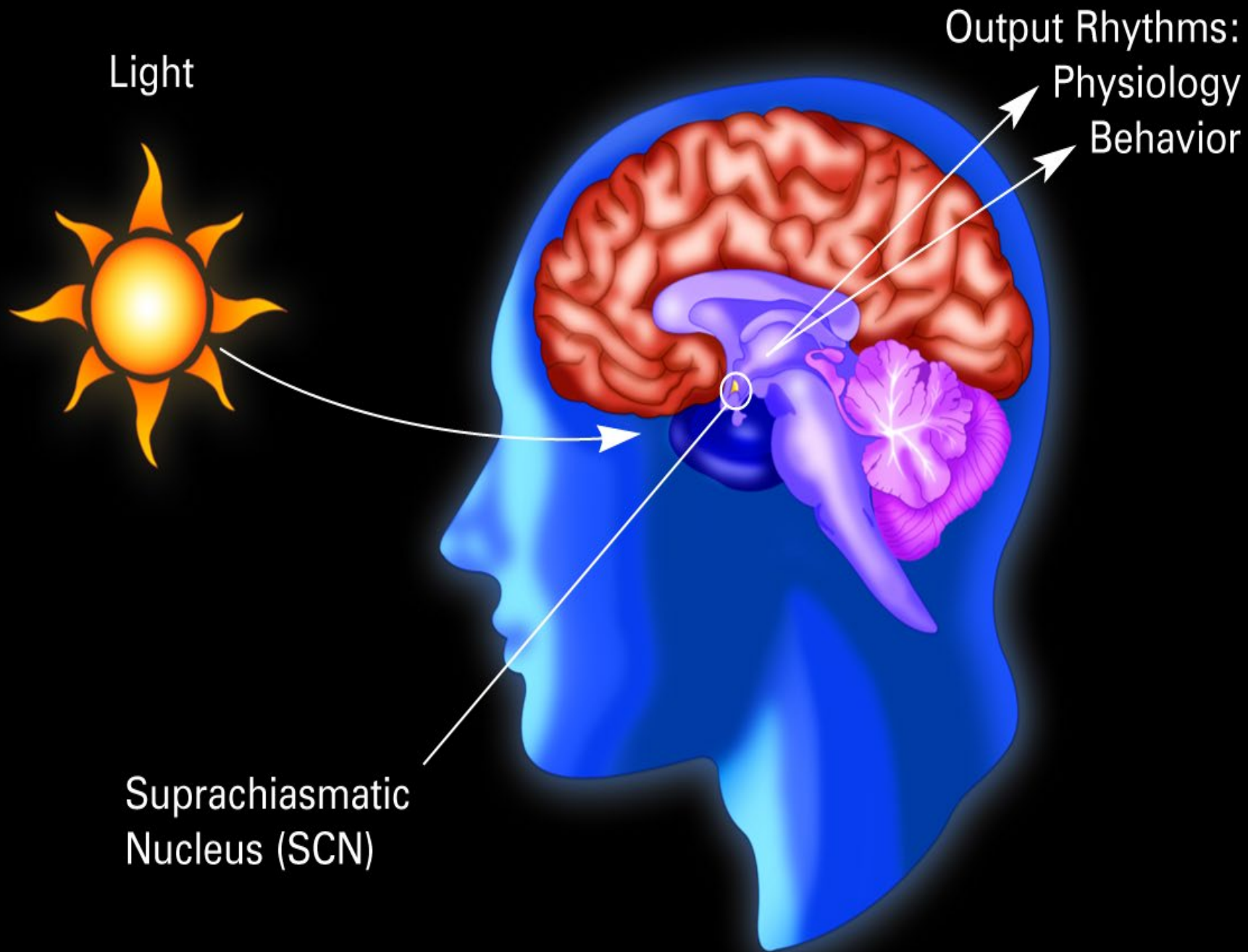
Homeostatic and circadian effects on wakefulness



Why do we sleep at night?

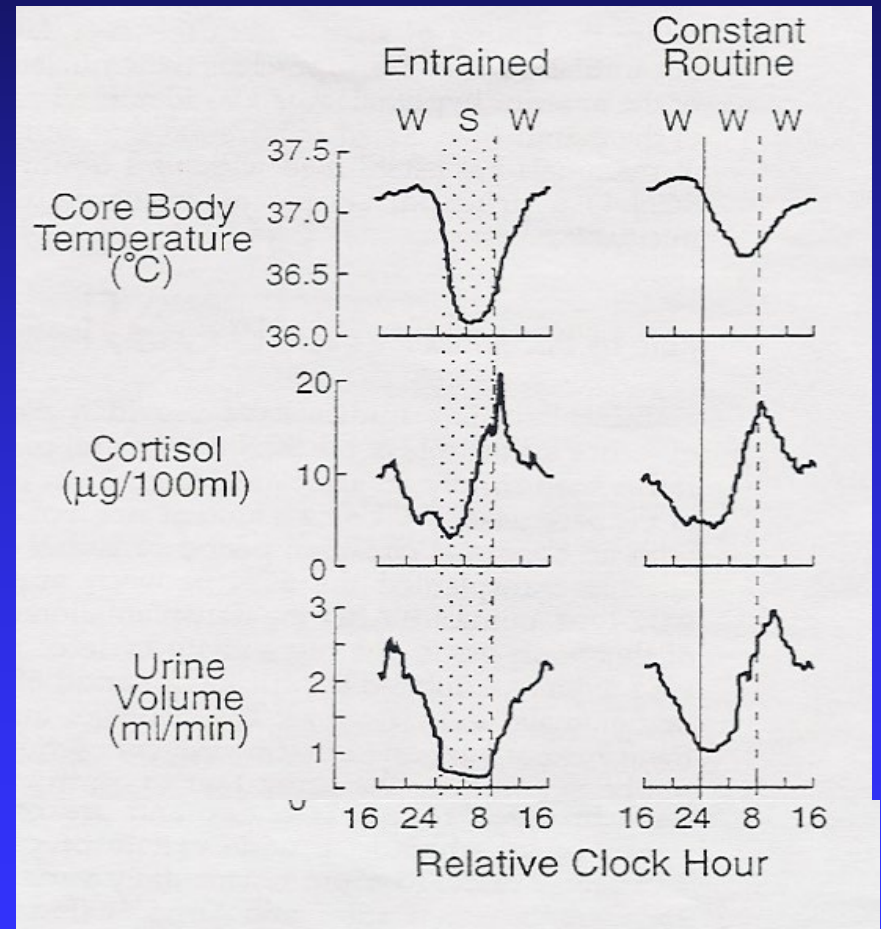
Biological rhythms in:

- ◆ Sleep and wakefulness
- ◆ Normal and abnormal EEG activity
- ◆ Urine output
- ◆ Body temperature
- ◆ Many, many hormones
- ◆ Endogenous rhythms with a period of ~24 hours are called circadian
- ◆ Other biological rhythms - ultradian (<24 hrs) , infradian rhythms (>24 hrs, i.e. menstrual cycle)



Circadian dependant functions

- Conditions of testing:
 - ◆ **Entrained** - sleeping at routine night-time hours
 - ◆ **Constant routine** – kept continuously awake and in the same body position in dim light
- Circadian dependent functions retain pattern even when an individual is continuously awake



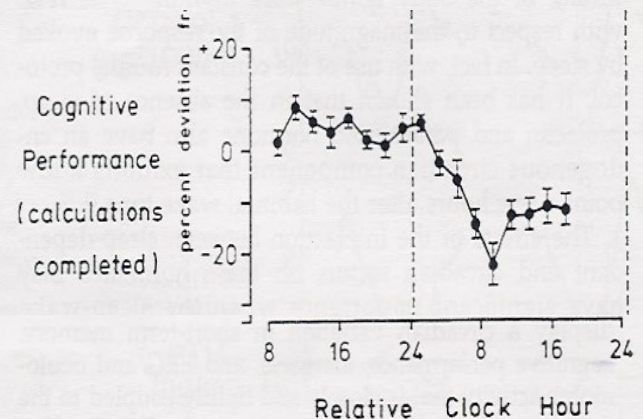
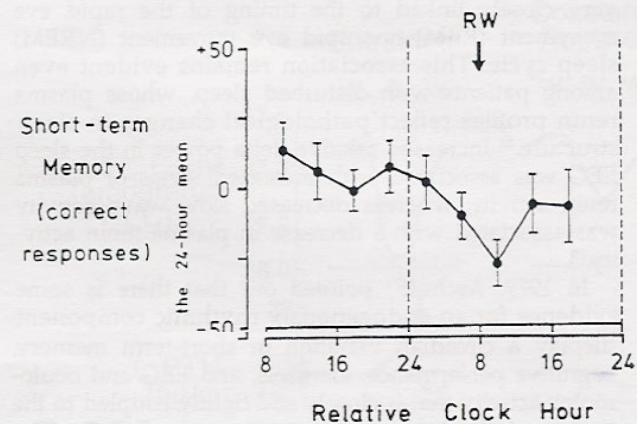
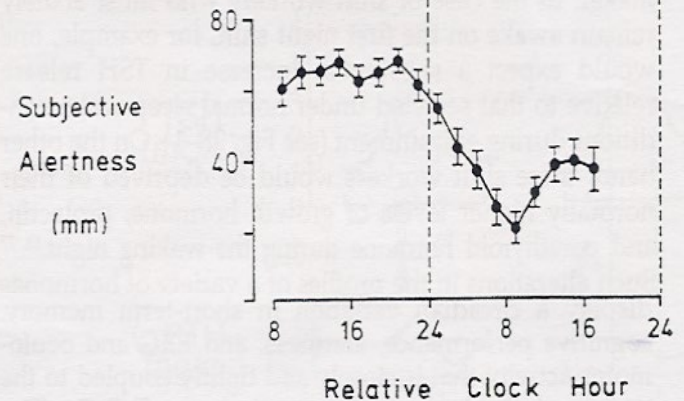
Circadian effects on alertness and cognition

Conditions of testing:

Entrained - sleeping at routine night-time hours

Constant routine – kept continuously awake and in the same body position in dim light

Alertness and cognition have a circadian pattern even in the absence of sleep at night



Gender Differences in Sleep

- Women tend to have:
 - ◆ slightly more slow wave sleep (13% vs. 9% in men)
 - ◆ less stage 1 sleep (8% vs. 11%)
 - ◆ possibly a greater sleep need
 - ◆ common sleep disorder present differently

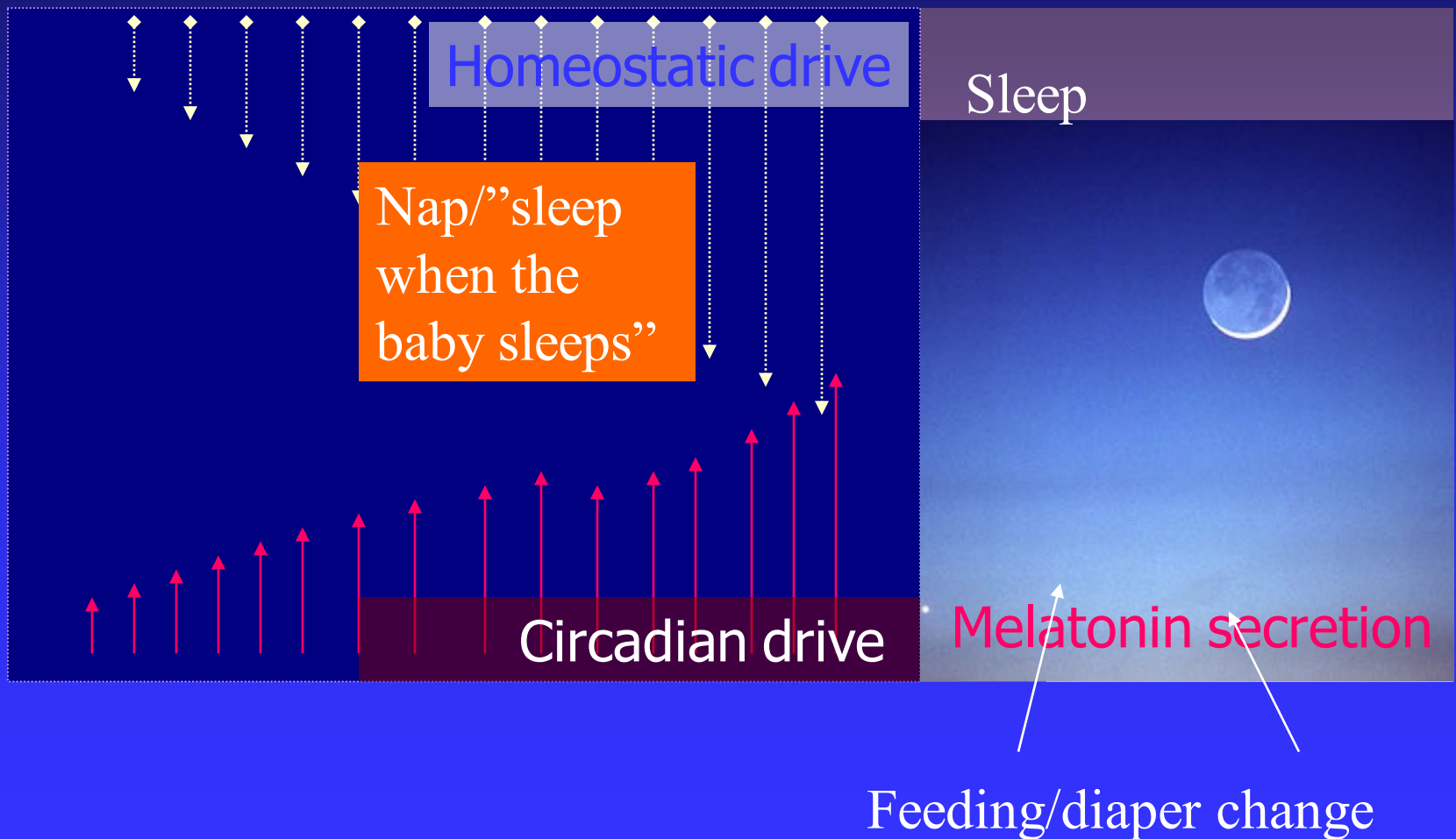
Pregnancy

- Modestly shorter REM latency
- Fragmented sleep – from various disruptors
- Proportion of slow wave sleep increases as pregnancy advances (36% in the last trimester vs. 26% in the first trimester)
- Common problems: insomnia, RLS, PLMD

- *A 37-year-old woman with severe insomnia*
- *Onset – after second pregnancy*
- *No childhood history of insomnia*
- *No prior complaints of disturbed sleep*
- *Sleep fragmentation with her first pregnancy*
- *During the second pregnancy, she again experienced similar difficulties, but they continued after the second delivery*
- *Typical bedtime - 11 p.m.*
- *When difficulty falling asleep, → lorazepam at around midnight*
- *No difficulties with sleep maintenance*
- *Typical wake-time - 7 in the morning*

- *PMH – epilepsy - 2 unprovoked generalized convulsions, both of which occurred at around 6 in the morning.*
- *lorazepam taken at times of aura to prevent generalized convulsions*
- *The patient was very concerned with the continuous and slowly increasing dose needed to achieve sustained sleep. A dose of 0.5 mg of lorazepam was initially sufficient to let her fall asleep, but after 4-5 months sleep became again problematic and the dose was increased to 1 mg and subsequent to that, she was told to take 2 mg if need be.*

Predisposed + provoked + perpetuated



- 1) Insomnia often can be provoked in predisposed individuals by a change in medical condition or lifestyle – both of which occurred in this case.
- 2) Effective treatments for insomnia may combine optimal sleep hygiene and medications.
- 3) The choice of medication should be individualized – pregnancy, lactation, family planning, as well as presence of other medical conditions should all be taken into account.

Treatment Considerations

- Condition (pregnant, lactating, or neither)
- Co-morbidities
- Other medications
- What other changes have occurred at the time insomnia started?
- Type of insomnia (sleep initiation vs. sleep fragmentation)
- Expected length of treatment

Treating insomnia during pregnancy

- Focus on behavioral techniques
- Most hypnotics are either category C or category D (either questionably safe or unsafe during pregnancy)
- Category B (probably safe) - antihistamines

Good Sleep Recommendations

- Discussion of optimal sleep need (~ 8 hours in most studies). A common maladaptive behavior is to stay in bed very long hours from fear of missing an opportunity to fall asleep.
- Discussion of diet agents and effect on sleep – including caffeine and alcohol, including in food additives, energy drinks, etc. As there are variations in the rate of metabolism for caffeine, generally for a bedtime of 10-11 p.m. It is recommended that the last caffeine drink is before noon-time.

- Explanation of circadian rhythms and their effect. A general rule is to have regular wake-time, ample amount of light during the day and dimmer light during the evening, thus allowing optimal entrainment.
- Stimulus control measures – including using the bed for sleep only.

Follow-up

- Over the next 24 months the patient
 - ◆ Improved her sleep hygiene
 - ◆ Became intermittently anxious that she will lose sleep, the sleep loss will provoke a seizure and that the convulsion may threaten her child
 - ◆ We discussed repeatedly the pro-s and con's of benzodiazepine use for insomnia in the setting of epilepsy
 - ◆ She met with a psychologist to discuss anxiety
 - ◆ We discussed strategies to optimize exercise – she did daily and intense exercise prior to the pregnancy

- With resuming exercise, insomnia gradually improved, the patient slowly tapered lorazepam
- 24 months after the initial visit she did not need lorazepam for sleep initiation

In the postpartum period

- Consider postpartum depression as a co-morbid factor
- Discuss lactation considerations
- Discuss daytime routine
- Consider how treatment will evolve over time

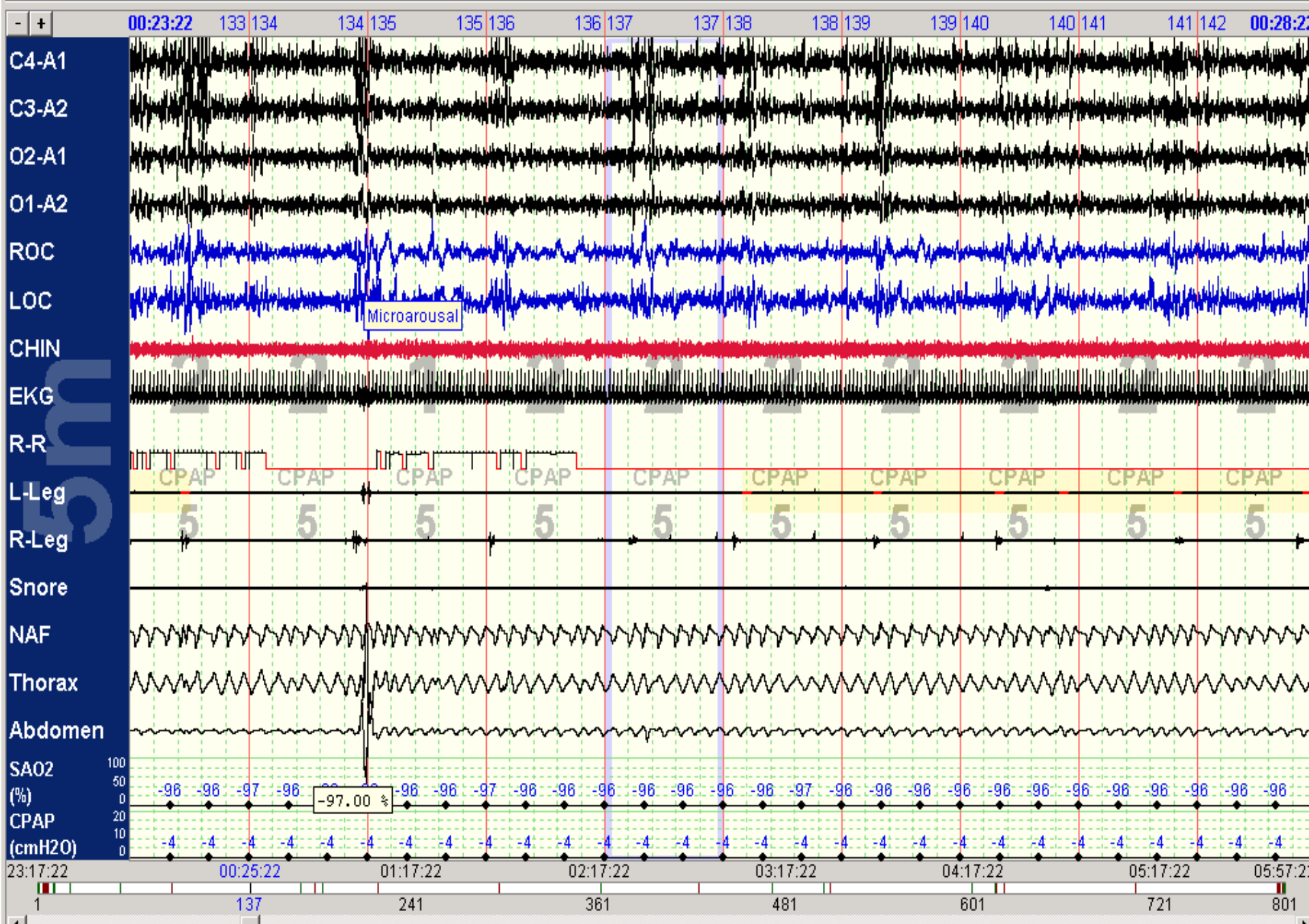
Discussion



- *Ms BB presented at age 40, and three months after giving birth to her second child, for symptoms of uncomfortable sensations of the lower extremities.*
- *Onset - during the second trimester of the pregnancy; continued post-partum.*
- *She had had similar experiences with her prior pregnancy, but those were self limited. The sensations involved both legs and were difficult to describe. Although not frankly painful, they were highly uncomfortable and prevented her from falling asleep.*
- *Further evaluation revealed a ferritin value of more than 50 ng/ml and a normal folate level.*
- *At the time of presentation, the patient was breast-feeding. After a thorough discussion, a decision was made to start medication treatment after breastfeeding ends with a dopamine agonist (pramipexole).*

Restless Legs Syndrome (RLS) and Periodic Limb Movements of Sleep (PLMS)

- RLS: indescribable uncomfortable sensations that make the patient move limbs
- PLMD – PLMS seen on PSG + symptoms (fragmented sleep, daytime sleepiness, etc.)
- Diagnosis: by history; PSG can give confirmation of PLMS
- Evaluation: other medical problems, sleep disorders, ferritin level



- **RLS is common in pregnant women.**
- In a study of 606 women - 26% had RLS: only 37% of them had RLS symptoms prior to the pregnancy
- Pre-existing RLS tends to indicate longer duration.
- Women with hereditary RLS may experience worsening during pregnancy
- Peak - third trimester of pregnancy

Manconi et al - Neurology. 2004 Sep 28;63(6):1065-9
Winkelmann J, et al- Sleep. 2000 Aug 1;23(5):597-602

- Frequently - dramatic improvement after delivery (within one month)
- RLS may be associated with insomnia
- RLS in pregnancy may be related to iron metabolism:
 - ◆ a low mean corpuscular volume and hemoglobin reported
 - ◆ Lower serum folate also may contribute

RLS/PLMS and neurological conditions

- Deriu et al, 2009 – 45 % patients with MS reported RLS symptoms
- Silvestri et al, 2007 – 26 % of children with ADHD had RLS symptoms
- Malow et al., 1997 – RLS may worsen sleepiness in patients with epilepsy as well as controls

RLS/PLMD treatment

- Dopamine-agonists or Levodopa
 - ◆ Pramipexole
 - ◆ Ropinirole
- Gabapentin
- Fe supplementation if indicated (Ferritin<50)
- Opiates and benzodiazepines have limited role

Treatment of RLS during pregnancy and puerperium

- Evaluation of ferritin, and folate levels
- If ferritin < 50 ng/ml, iron supplementation until >100
- Folate supplementation should be considered.
- Other pharmacological treatment should consider pregnancy status
- Follow up for any side effects, some of which are rare.

Considerations with common RLS medications

- Gabapentin, ropinirole and pramipexole are all pregnancy category C
- Animal data suggests potential teratogenic effects from ropinirole, less is studied on pramipexole
- Pramipexole may lower serum prolactin [Schilling et al 1992]
- Gabapentin and Ropinirole may be secreted in human milk

Compulsive behaviors

- From a questionnaire based study:
 - ◆ 10% - compulsive shopping,
 - ◆ 7% - compulsive gambling,
 - ◆ 23% - compulsive eating

Summary

- 1) RLS commonly starts in pregnancy and may persist after delivery
- 2) RLS is often associated with low ferritin level and anemia during pregnancy may be one predisposing factor
- 3) In pregnancy, RLS can be also associated with low folate level
- 4) Treatment of RLS and PLMD can be complicated as dopamine agonists may affect fetus and lactation

Follow-up

- *Symptoms improved,*
- *A dose of 0.5 mg/day treatment continued*
- *After 2 years the medication was stopped due to report of compulsive behaviors.*

Discussion



Dreams and Nightmares

- Pregnant women reported more dreams depicting themselves as a mother or with babies/children than non-pregnant women
- Nightmares in general are frequent in women, more than in men
- Frequent in pregnant women

- More pregnant women (21%) than non-pregnant women (7%) reported a nightmare incidence exceeding moderately severe pathology ($>1/\text{week}$) ($P=0.03$).
- Pregnant women also reported overall lower sleep quality ($P=0.007$) and
- more night awakenings ($P=0.003$).
- Higher prospective recall of bad dreams ($r = -0.40$, $P=0.002$) and nightmares ($r = -0.32$, $P=0.001$) both correlated with lower sleep quality in pregnant women.*
- Prazosin is used frequently for nightmare treatment, but category C

*Lara-Carrasco et al *Sleep Med* 2014

- CC was a 30-year-old woman with insomnia, that started simultaneously with severe daily headaches that started relatively abruptly during the second trimester of her pregnancy. Usual bedtime was at around 10 p.m. She described herself as restless but did not snore frequently or loudly. Her wake-time was 6:30 or 6:45 when her baby awakened. She felt tired throughout the day and took naps whenever possible. Her headaches were worst in the morning, though present throughout the day.

- The patient's medications included weaning doses of morphine sulfate controlled-release and oxycodone and acetaminophen, as well as duloxetine. Past medications include propranolol and zonisamide as well as amitriptyline. Regarding sleep, she has taken zaleplon with no effect, and cyclobenzaprine for muscle relaxant with no effect on sleep, and tizanidine, which improved sleep.

- Physical exam was notable for a BMI of 29.5 (the patient was overweight) and a mildly narrowed upper airway.
- The patient was evaluated with a polysomnogram performed prior to this visit, which showed a respiratory disturbance index of 18 events per hour, but a lot of the events were central. She had 11 central apneas and 93 hypopneas, and thus, it was hypothesized during the sleep study that a lot of her hypopneas probably are also central.

Discussion points

- 1) Pregnancy may affect other conditions, which in turn worsen sleep
- 2) Medications used to treat pain may lead to central apnea and thus further disrupt sleep
- 3) Poor sleep may exacerbate pain, forming a vicious cycle
- 4) A thorough evaluation is warranted, as disturbed breathing may be associated with complications in pregnancy.
- * morning headache can be seen in 18-74% of patients with OSA and may respond to OSA treatment

- More than a third of pregnant women report pathologic sleepiness with an Epworth sleepiness score of more than 10
- 23 % of pregnant women may be at high risk for OSA
- the risk reaches 66% in complicated pregnancies
- obstructive sleep apnea may contribute to a higher risk of hypertension during pregnancy
- Pregnant women with OSA have
 - ◆ more than twice higher risk for preeclampsia
 - ◆ preterm birth
 - ◆ more likely to need cesarean section

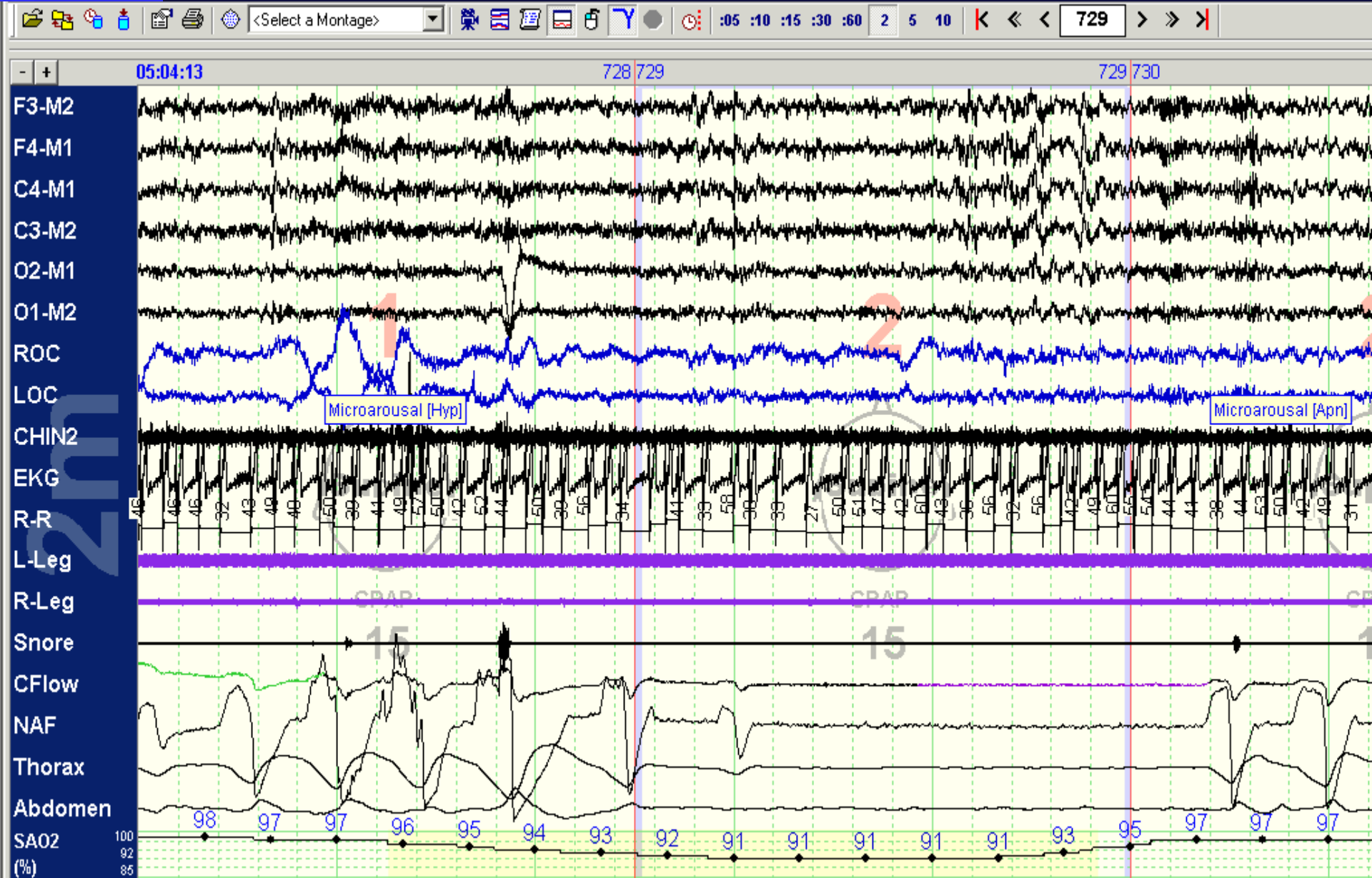
Followup

- Based on the association of OSA with hypertension, treatment of preeclampsia with CPAP was proposed and evaluated.
- Nasal CPAP in addition to standard prenatal care, compared to standard prenatal care alone for hypertensive pregnant women in a randomized controlled trial - a steady increase in blood pressure and dose of antihypertensives in the group without CPAP

Central apneas

- Chronic opioid use predisposes to central sleep apnea with approximately 30% of the patient developing this phenomenon
- Walker et al report a six-fold increase in the rate of central apneas per hour in patients taking opioids, as well as lower oxygen saturation
- The degree of sleep disordered breathing in such cases may be dose dependent

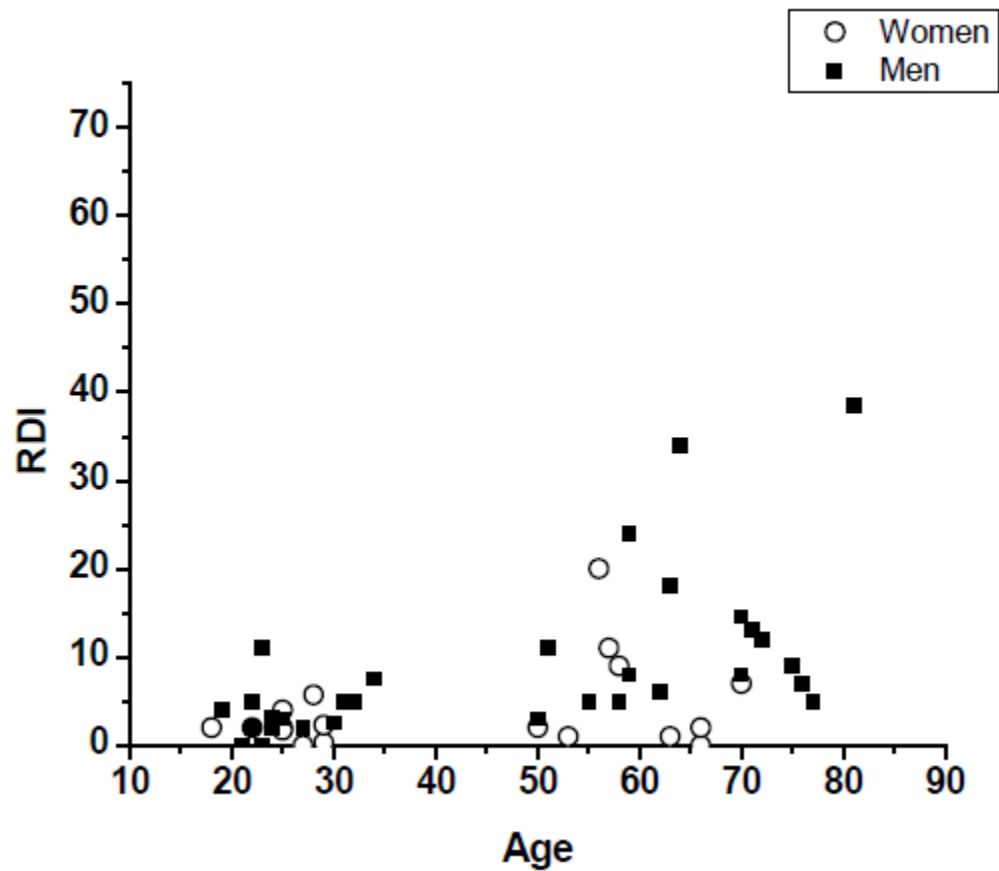
Central apnea



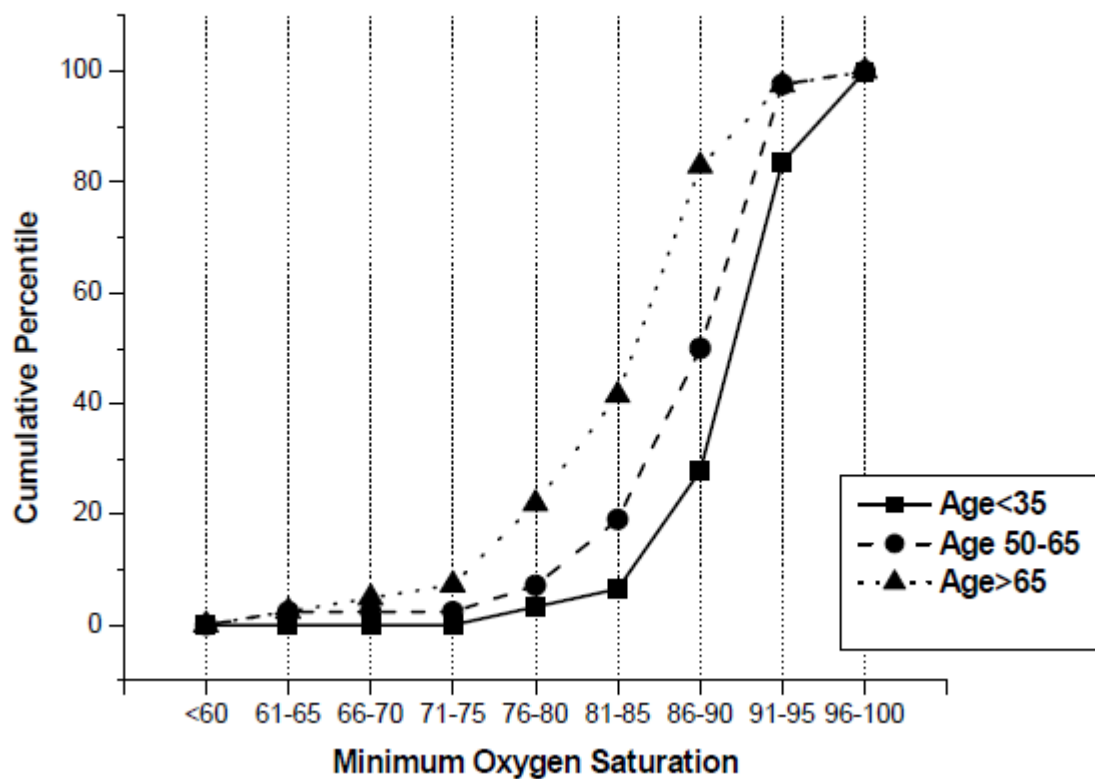
Discussion



RDI by age – non-sleepy, non-overweight



Minimum oxygen saturation by age – cumulative percentile



Non-surgical ways to treat OSA



