



The pain and sleep interaction

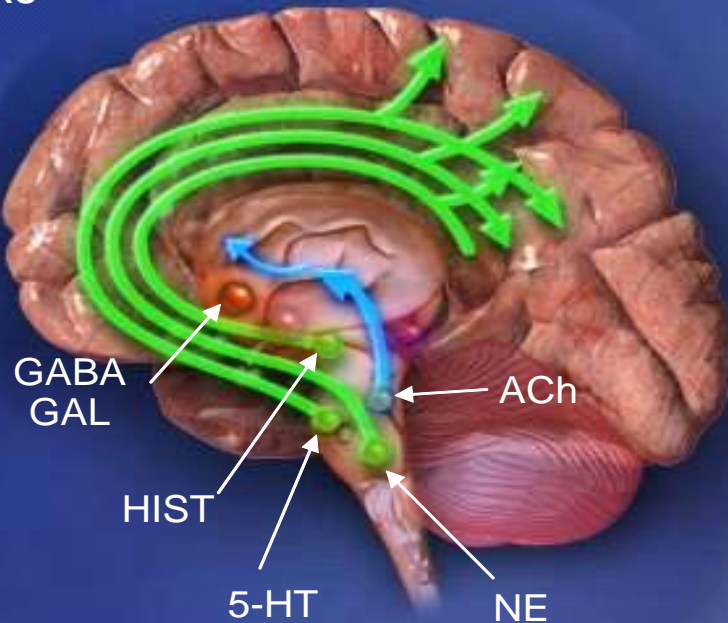
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Sleep and trauma; Hôpital du Sacré Cœur de
Montréal

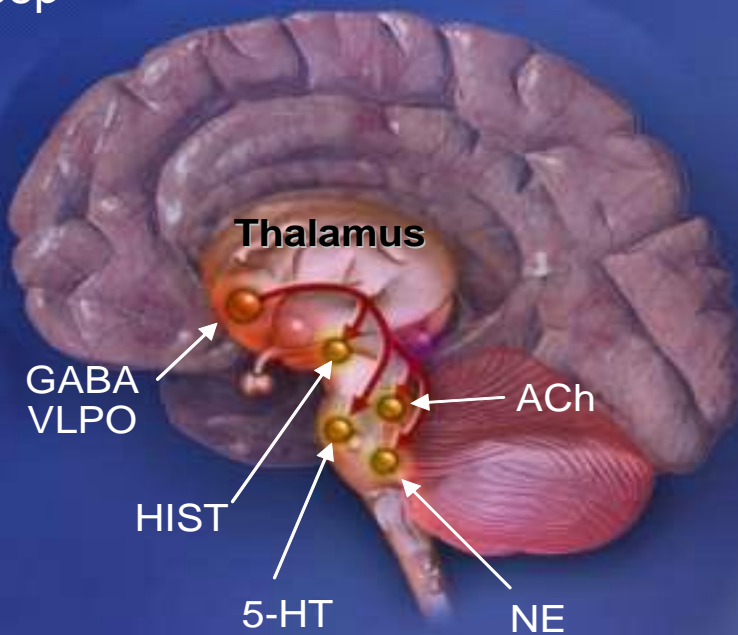
Speaker or consultant for:

- Wyeth-Pfizer, Canada
- UCB, Belgique
- Sanofi Aventis, Canada et France
- Grindcare, Danemark
- Respironics, USA
- Oral appliance for sleep disorders: Narval, Fr;
Silencer, Cdn
- No trade market share or direct \$ investment, etc

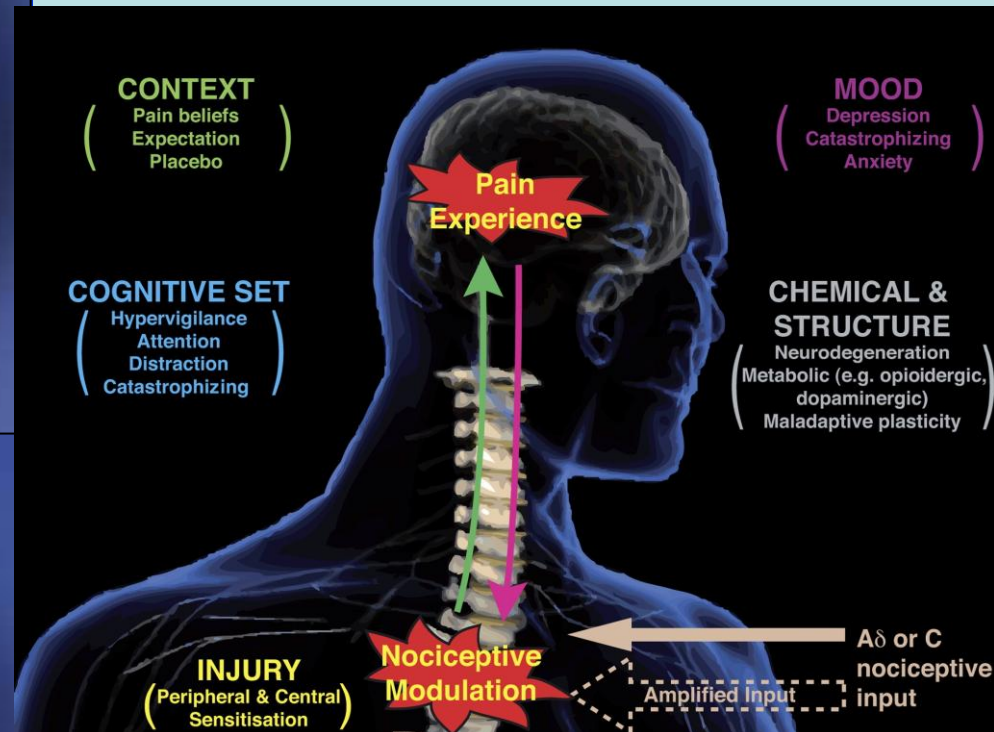
Awake



Asleep



Sleep is a physiological and behavioural state with a partial isolation from the external milieu

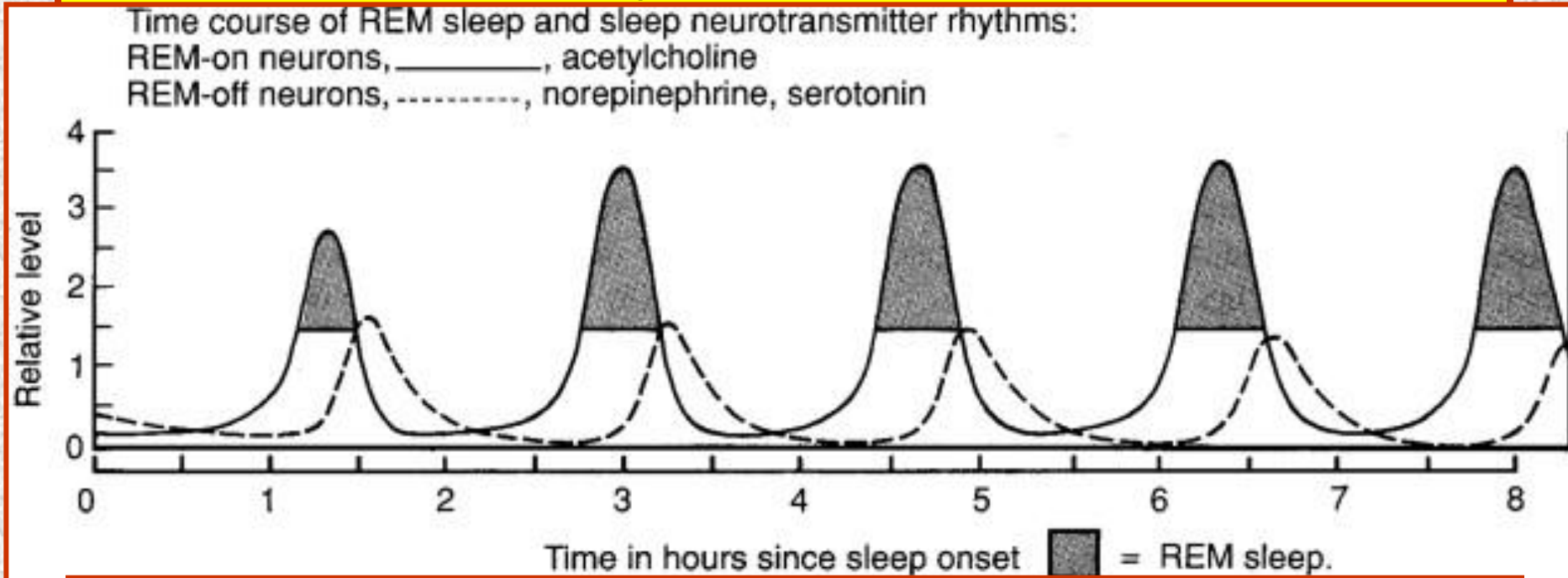


Pain = hypervigilance

Saper 2001, Trends in Neurosc; Lavigne 2005, in Principles Practice Sleep Med, Kryger et al eds, Elsevier; Tracey 2007

Ach, 5Ht and Ne fluctuation across nonREM and REM

ultradian sleep cycles- McCarley 2007 Sleep Med



WAKE **Non REM** **REM**

Monoamine
(DA, NE, 5HT)

+++

+

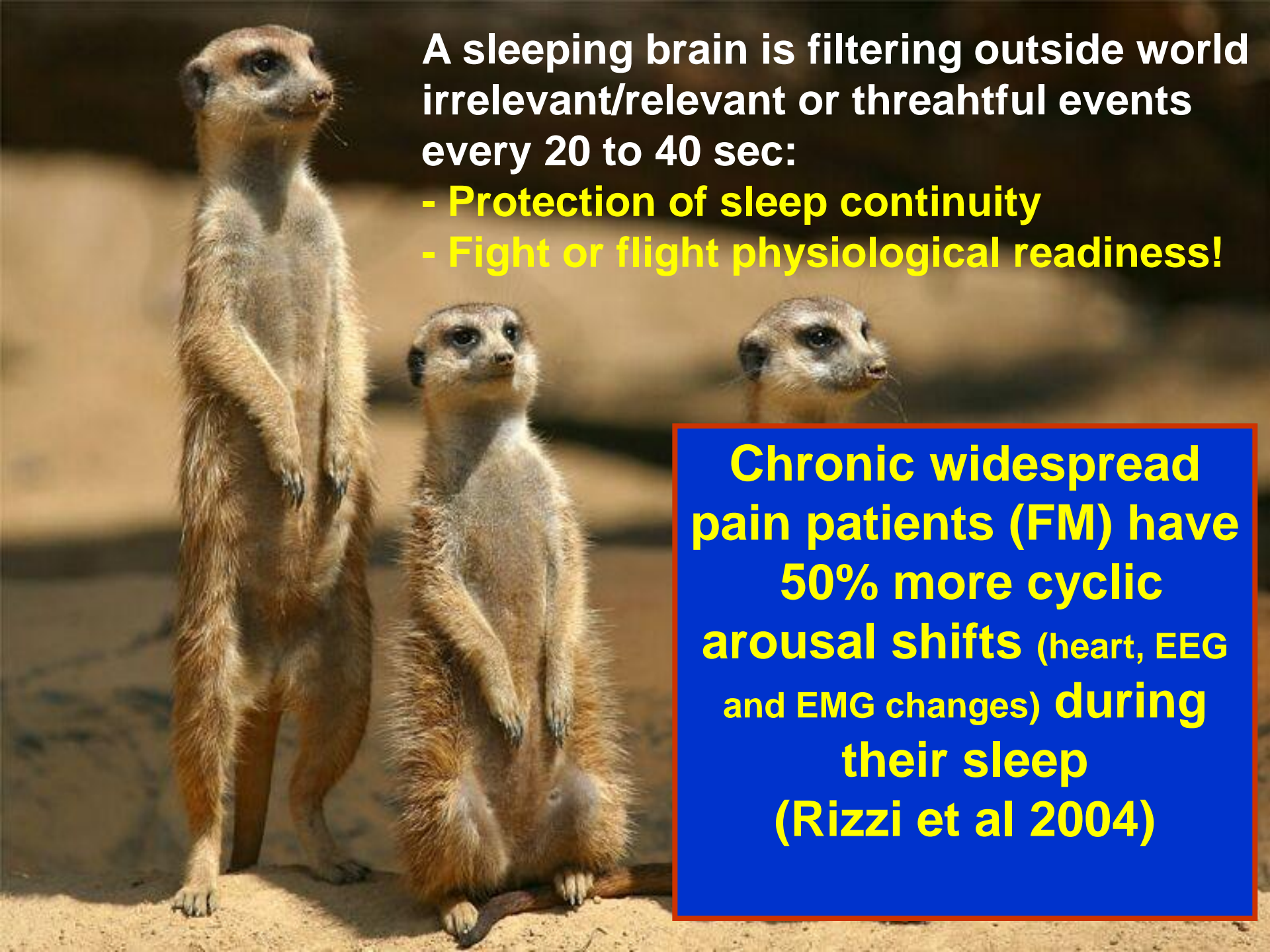
LOW

Acetylcholine

+++

Low

HIGH



A sleeping brain is filtering outside world
irrelevant/relevant or threahtful events
every 20 to 40 sec:

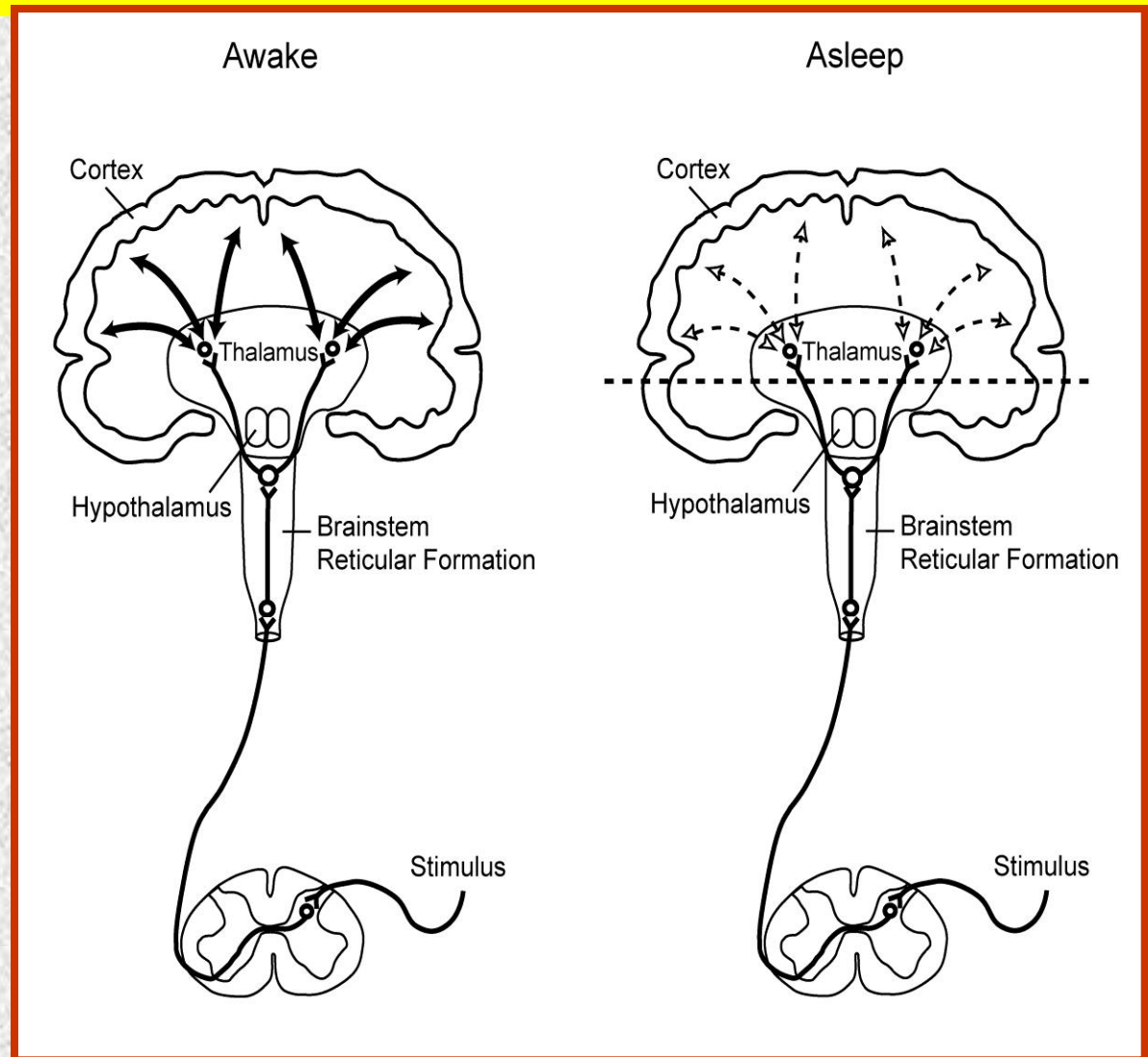
- **Protection of sleep continuity**
- **Fight or flight physiological readiness!**

**Chronic widespread
pain patients (FM) have
50% more cyclic
arousal shifts (heart, EEG
and EMG changes) during
their sleep
(Rizzi et al 2004)**

Cortical and brainstem networks are **PARTIALLY** isolated *from peripheral inputs* to preserve sleep continuity / homeostasis against *Fight or Flight activations* (Saper, TENS 2001; Lavigne, 2007)

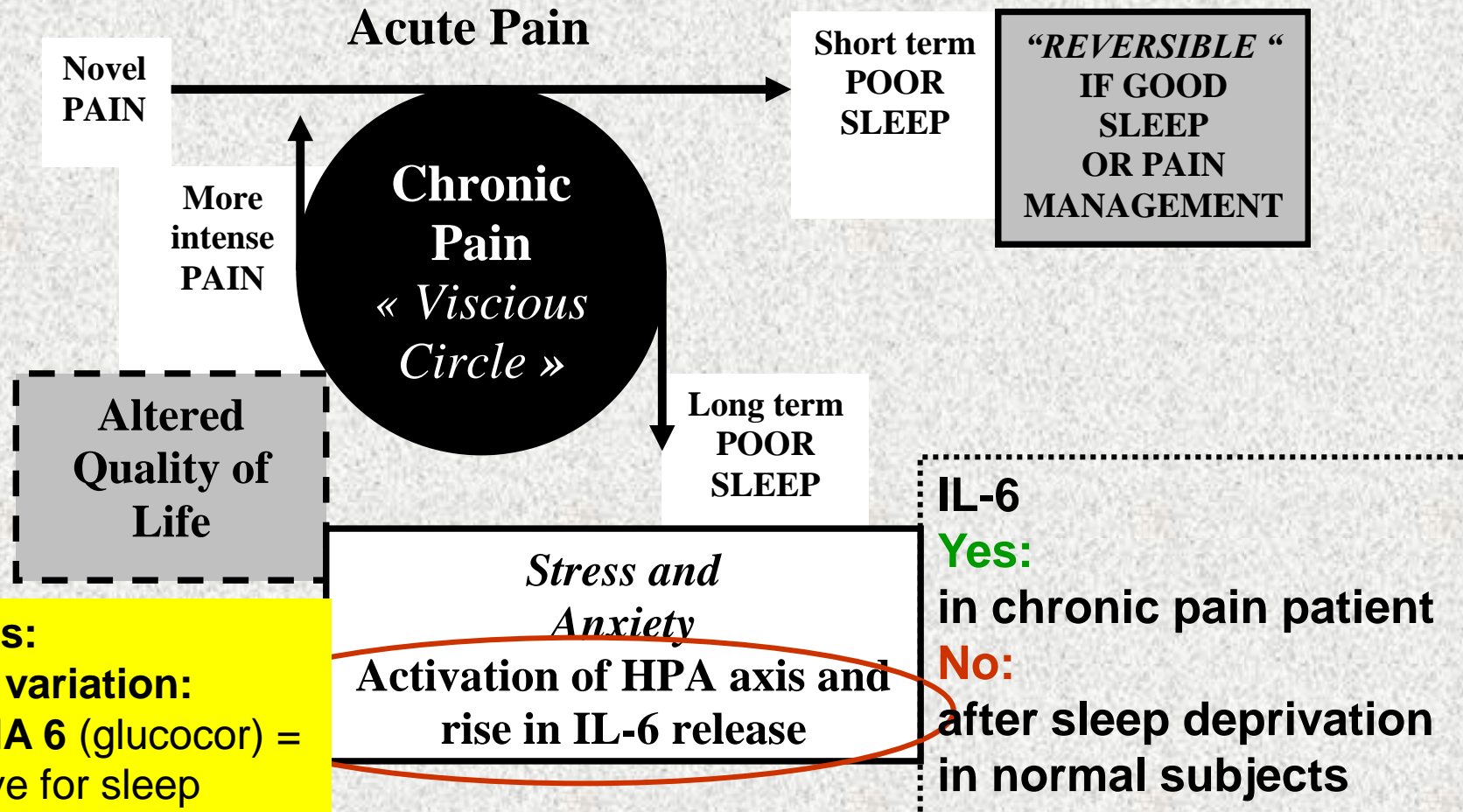
**Thalamo-cortical
GATING and
AROUSAL**

3-10 sec
EEG, HR, EMG
rises



RELEVANCE OF SLEEP AND PAIN INTERACTION

Linear and Circular effects of pain on sleep



Lavigne, Principles & Pract Sleep Med, 2005 - Elsevier book

McBeth, Arthritis & Rheuma 2007; Haack, Sleep 2007; Holliday, Ann Rheuma Disor; Older 1998

PAIN & SLEEP: linear or circular interaction?

Acute pain precedes poor sleep complaints =
linear relationship

e.g.: new pain experience precedes poor sleep \approx
50 - 89% of cases (Morin 1998; Smith 2000; Riley 2001)

With chronic pain, a **circular relationship** seem to
dominates:

*a night of poor sleep is followed by more
variability in pain reports and a day with pain
with a less recuperative sleep*

▶ **Day with pain = poor sleep** (28% of variance)

▶ **Poor sleep = more pain the next day** (5% of variance)

(Affleck 1998; Raymond 2001; Riley 2001; Nicassio 2002)

- In **older** musculoskeletal pain patients, better
sleep= lower pain (n=50, + 60 y.o.; Dzierzewski et al 2010)

PAIN & SLEEP: linear or circular interaction?

When pain is chronic, a **circular relationship seem to dominates BUT...**

INSOMNIA impact on such outcomes

(Prevalence: 10% general pop; up to 30% in chronic pain patients)

- **Initial insomnia induce significant rise in pain over time (explain 16% of the variability; Temporomandibular pain, n=53; Quartana et al, PAIN 2010)**

Chronic pain = Deprivation of sleep or Non Restorative Sleep?

- Non restorative sleep (NRS)

10% pop (Ohayon 2005) =

Sleep is restless, light or of poor quality.

Link to sleep duration and disorders in many cases!

NRS is further define as (Stone 2008) =

Persistent feeling of un-refreshing sleep upon awakening not due to lack of sleep

Chronic pain = Non Restorative Sleep or sleep restriction (shorter duration)?

- About **2/3 of patients with chronic pain** also complain of **poor sleep quality and/or un-refreshing sleep sensation**
- This is reported by about 50% of orofacial patients and up to 70% OA & 60-90% of *fibromyalgia (FM)*- **chronic widespread pain (CWP)** patients

The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity

FREDERICK WOLFE,¹ DANIEL J. CLAUW,² MARY-ANN FITZCHARLES,³ DON L. GOLDENBERG,⁴ ROBERT S. KATZ,⁵ PHILIP MEASE,⁶ ANTHONY S. RUSSELL,⁷ I. JON RUSSELL,⁸ JOHN B. WINFIELD,⁹ AND MUHAMMAD B. YUNUS¹⁰

Results. Approximately 25% of fibromyalgia patients did not satisfy the American College of Rheumatology (ACR) 1990 classification criteria at the time of the study. The most important diagnostic variables were WPI and categorical scales for cognitive symptoms, unrefreshed sleep, fatigue, and number of somatic symptoms. The categorical scales were summed to create an SS scale. We combined the SS scale and the WPI to recommend a new case definition of fibromyalgia: (WPI ≥ 7 AND SS ≥ 5) OR (WPI 3–6 AND SS ≥ 9).

Conclusion. This simple clinical case definition of fibromyalgia correctly classifies 88.1% of cases classified by the ACR classification criteria, and does not require a physical or tender point examination. The SS scale enables assessment of fibromyalgia symptom severity in persons with current or previous fibromyalgia, and in those to whom the criteria have not been applied. It will be especially useful in the longitudinal evaluation of patients with marked symptom variability.

WPI: Widespread Pain Index

BEST PREDICTORS are:

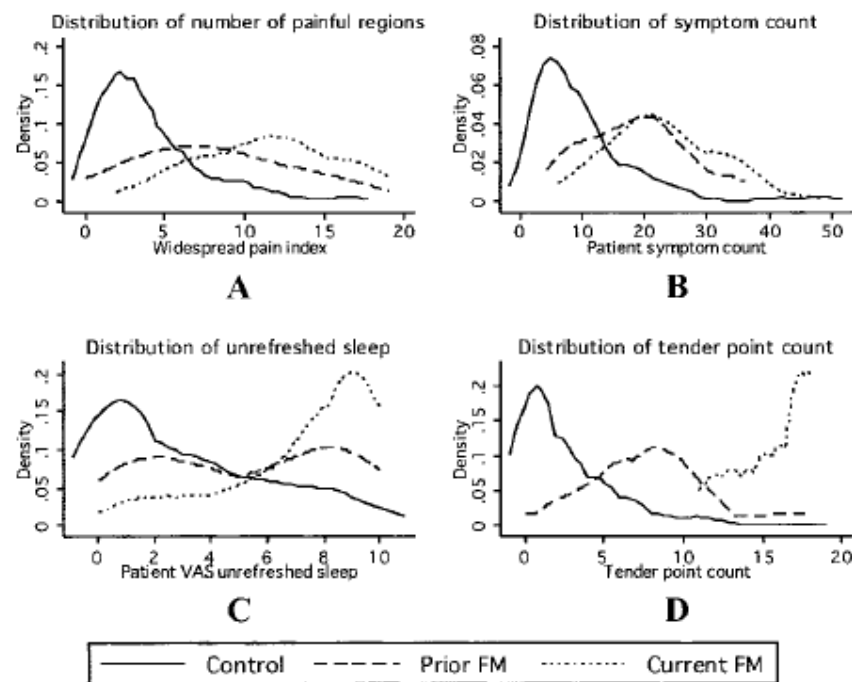
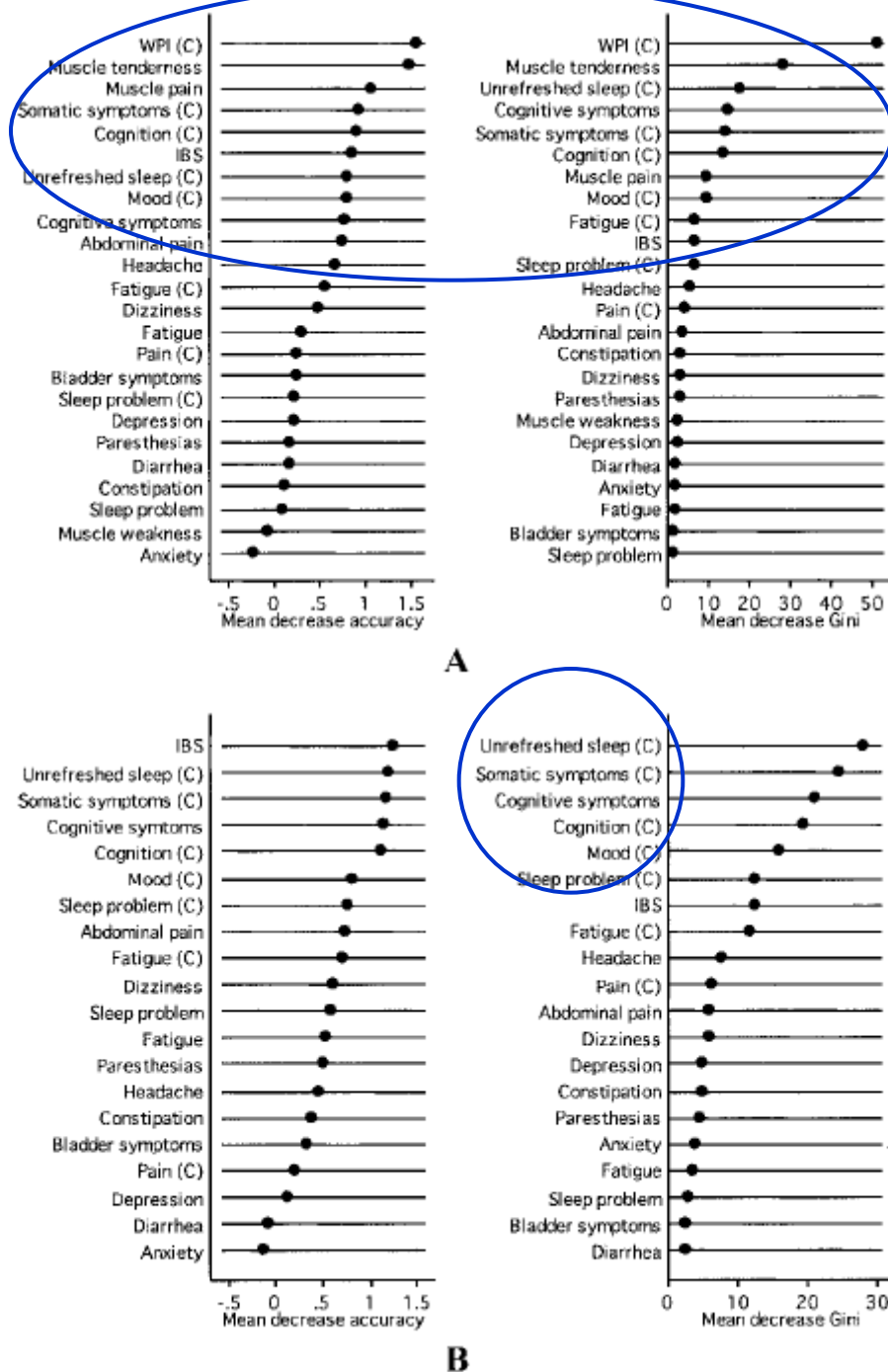


Figure 1. Distribution of key fibromyalgia (FM) variables in controls and patients with current or prior FM (phase 1). VAS = visual analog scale.

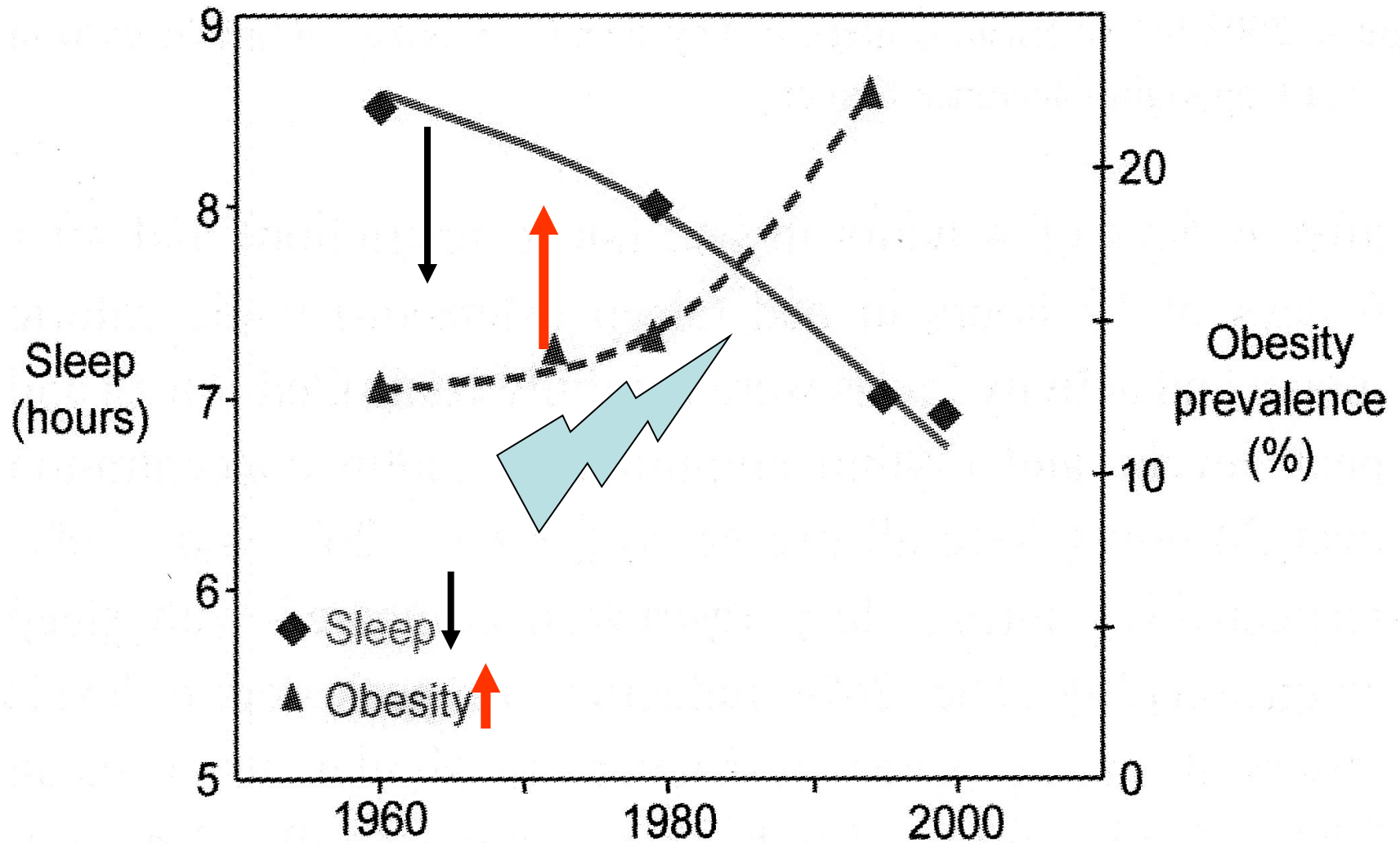


SLEEP DURATION (concept of restriction) seem to be a good predictor of next day pain

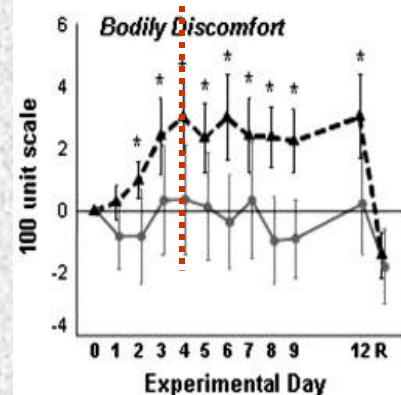
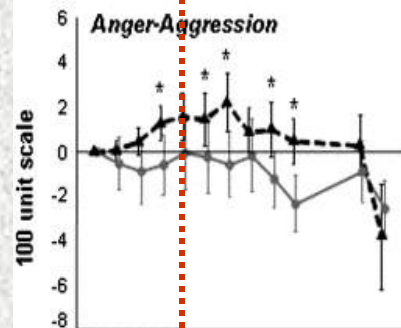
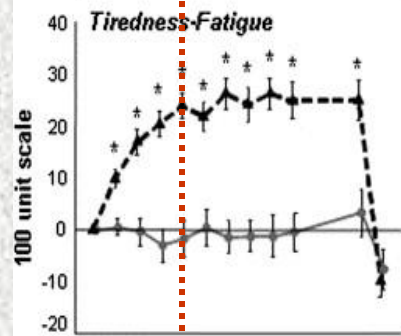
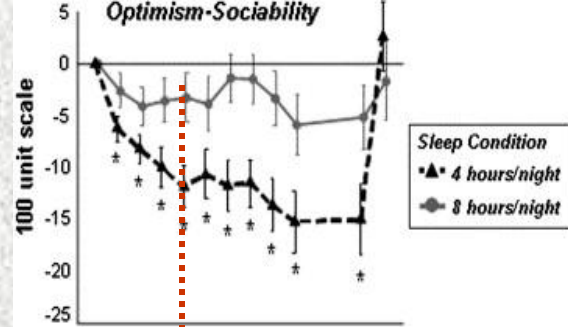
- ***If sleep is less than 6 hrs or more than 9 hrs = greater report of pain on next day*** (Edwards et al, Pain, 2008)

BUT in sleep medicine a CONTROVERSY is present regarding *too short or too long sleep duration vs. RISK of higher morbidity* (Hublin, Sleep 2007; Meisinger, Sleep 2007)

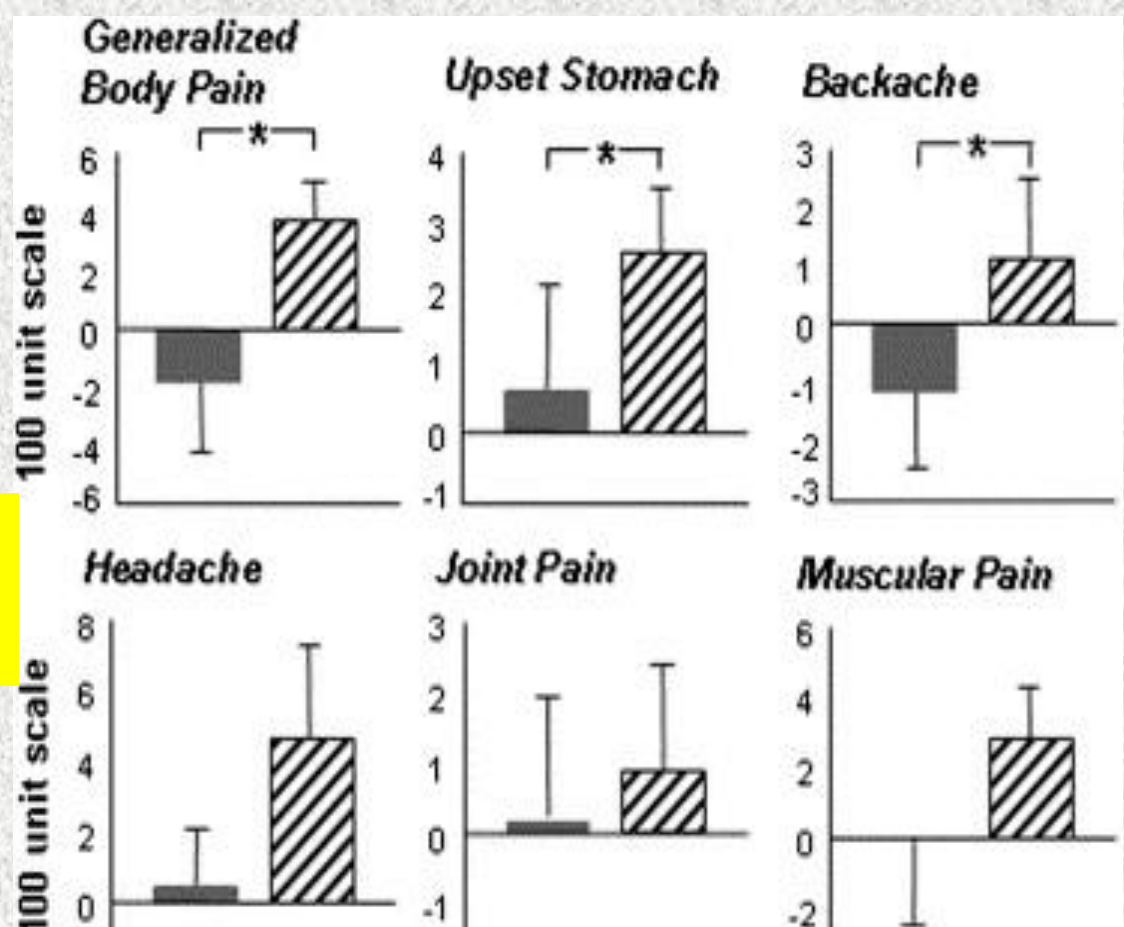
Reduction of sleep time & rise in obesity: coincidental or cause & effect?



Van-Cauter, Medscape Neurology & Neurosurgery 2005



**4 vs. 8 h
Normal
subjects**



THRESHOLD of 3 to 4 nights of Sleep Restriction
 (4 hr instead of 8 hr) =
MOOD influences & somatic *Pain* complaints
 Haack and Mullington, Pain 2005

CLINICAL PAIN = MAJOR SOURCE OF SLEEP LOST / Chronic Widespread Pain clinical population

- 1- 60 min less total sleep time (Polygraphy- PSG)
 - 2- lower efficiency of sleep (% time asleep/time in bed),
 - 3- 3 instead of 4-5 sleep cycles
 - 4- Long delay to fall asleep (33 min) and many PLM
- (see Drewes et al 1995 FM, 1998 RA; Okura et al, Sleep Med 2008)

Demographics and sleep variables of normal subjects, PLMS/RLS, insomnia and chronic widespread pain (CWP) patients

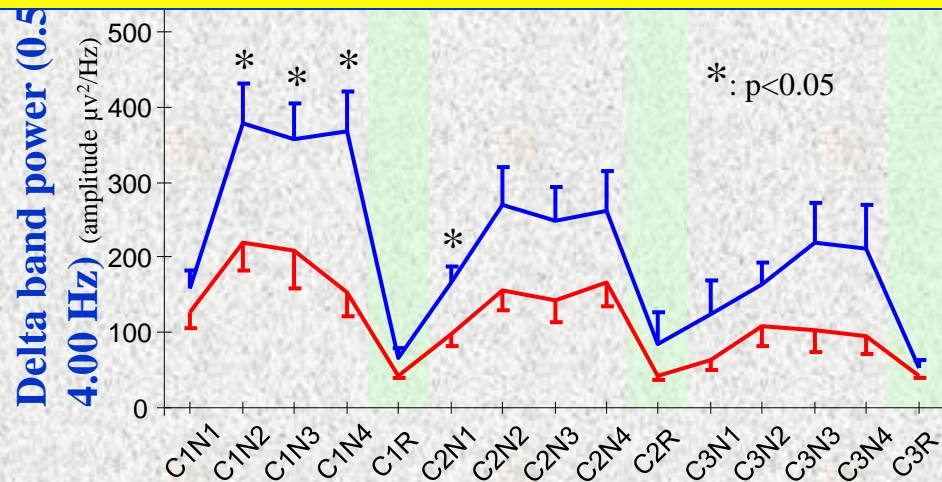
Variables	Normal subjects <i>a</i>	PLMS/RLS patients <i>b</i>	Insomnia patients <i>c</i>	CWP patients <i>d</i>	<i>p</i> -value group effect	<i>p</i> -value post-hoc test
I. Demographics						
Sex distribution	5F; 5M	5F; 5M	5F; 5M	8F; 9M		
Age	54.9 ± 3.2	55.9 ± 3.1	56.1 ± 3.1	54.8 ± 2.4	0.98	
II. Sleep variables						
Sleep duration [min]	436.5 ± 10.3	411.7 ± 12.5	381.5 ± 11.2	362.0 ± 19.6	0.01	0.01 ^{a-d}
Sleep efficiency [%]	91.2 ± 1.5	88.1 ± 1.6	81.1 ± 2.0	80.1 ± 2.8	0.006	0.05 ^{a-c} , 0.01 ^{a-d}
Sleep cycle	4.4 ± 0.2	3.4 ± 0.3	4.5 ± 0.4	3.7 ± 0.3		
Sleep latency [min]**	11.2 ± 2.0	24.8 ± 10.8	17.5 ± 2.8	33.4 ± 10.8		
REM latency [min]*	87.5 ± 10.6	120.4 ± 27.8	76.7 ± 11.7	109.9 ± 27.8		
Awakenings/h*	5.1 ± 0.8	5.7 ± 0.9	6.9 ± 0.8	7.1 ± 0.9		
Micro-arousals/h	9.6 ± 1.6	11.7 ± 1.9	10.8 ± 0.9	9.1 ± 1.6		
Sleep stage shifts/h**	33.6 ± 4.2	31.6 ± 4.1	27.3 ± 3.5	32.3 ± 4.2		
Stage 1 [%]	11.2 ± 1.6	12.9 ± 2.2	13.9 ± 2.0	11.0 ± 1.6		
Stage 2 [%]	61.9 ± 1.9	64.4 ± 2.1	61.5 ± 2.0	65.8 ± 2.1		
Stages 3 and 4 [%]**	7.0 ± 2.6	5.8 ± 2.6	3.3 ± 1.9	5.3 ± 2.6		
REM [%]	19.8 ± 1.3	16.9 ± 1.3	21.3 ± 1.8	17.5 ± 1.7	0.29	
PLMS index**	2.0 ± 0.9 (9)	33.4 ± 3.4	1.7 ± 0.8	8.8 ± 3.2	<0.001	<0.001 ^{b-a,c,d}

GENDER SPECIFICITY
Female CWP/ctl =
25% less REM time
Female CWP/male CWP=
2.6 X less Stages 3&4

Alpha-delta sleep: is not specific to pain,
not a biomarker and not pathognomonic

Control vs. CWP

Lower power of EEG Slow Wave Activity in CWP patients

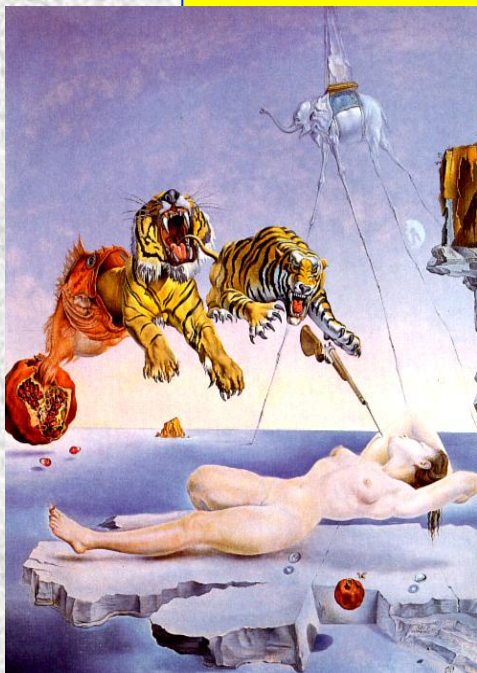
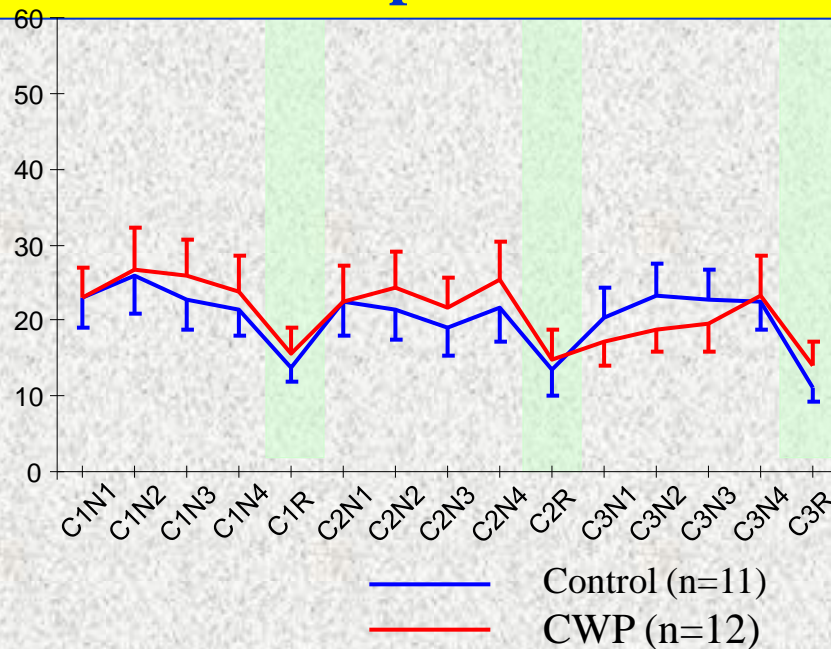


In Female only
not in Male patients
Lavigne, Sleep Med in press

Control vs. CWP

Alpha intrusions not specific to CWP

Alpha band power (8.00-13.00 Hz) (amplitude $\mu\text{V}^2/\text{Hz}$)



SLEEP DEPRIVATION

**(removal of a given sleep stage or a section of sleep
such a 2 hours sleep delay)**

Experimental PARADOX related to evidences in psychophysiological studies (quantitative sensory testing: QST; thermal, pressure algometers)

Most studies on sleep deprivation and pain were done in NORMAL subjects, under acute protocols and used model to assess HYPERALGESIA (see Lautenbacher reviews in 2006, 2007)

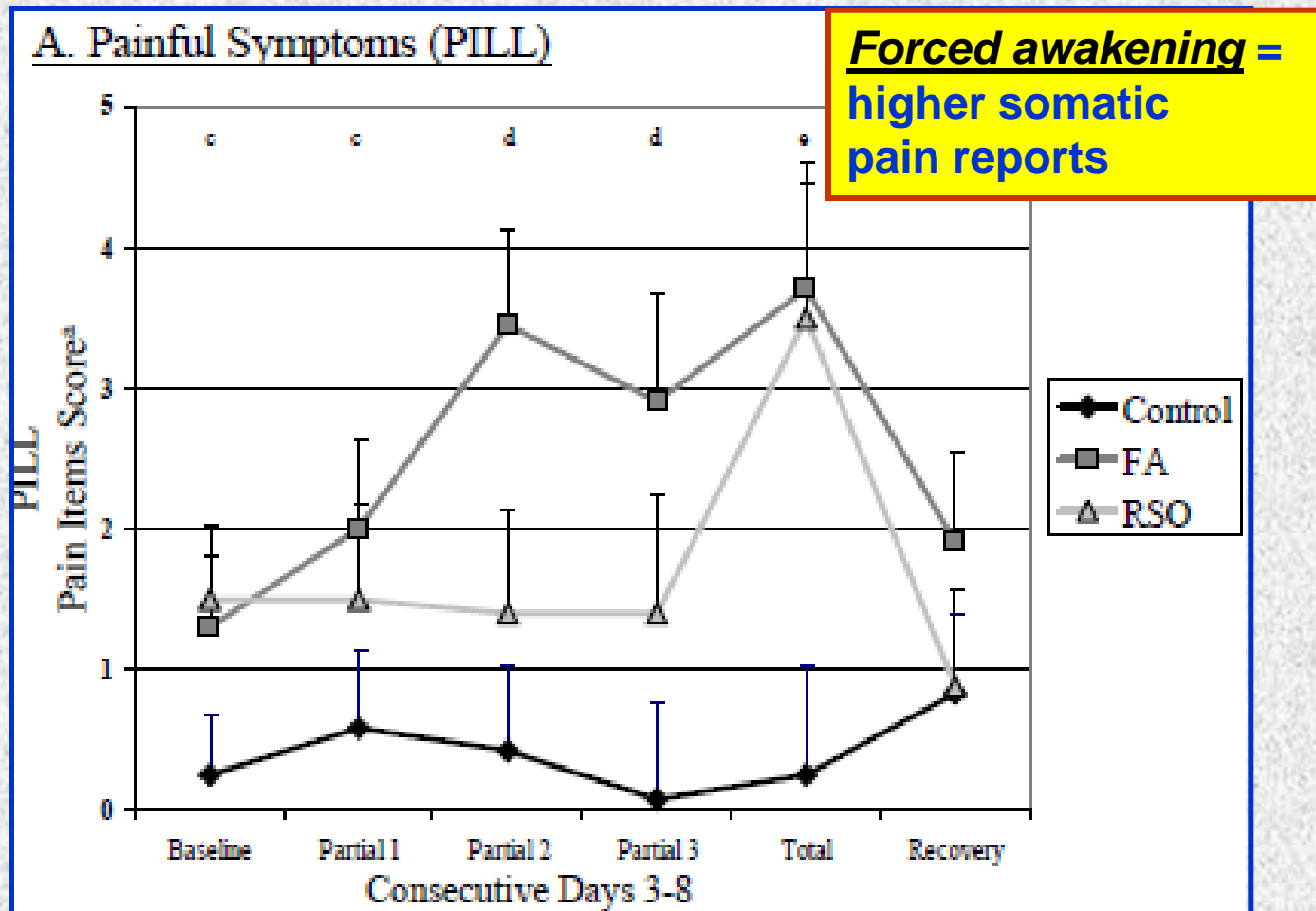
FM/CWP PATIENTs do suffer of several pain (diffuse/widespread) and sleep related problems and it is ALLODYNIA, not hyperalgesia alone that is probably critical

**Threshold studies =
first time heat or pressure is
perceived as painful (50% of time)**

**Pain tolerance studies =
max can be supported before OUCH!**

Disturbance of SLEEP CONTINUITY may be more important:

Forced awakening **FA** (blocks of 60 min sleep / wake) vs. Restricted sleep (delayed sleep onset) in **NORMAL SUBJECTS**

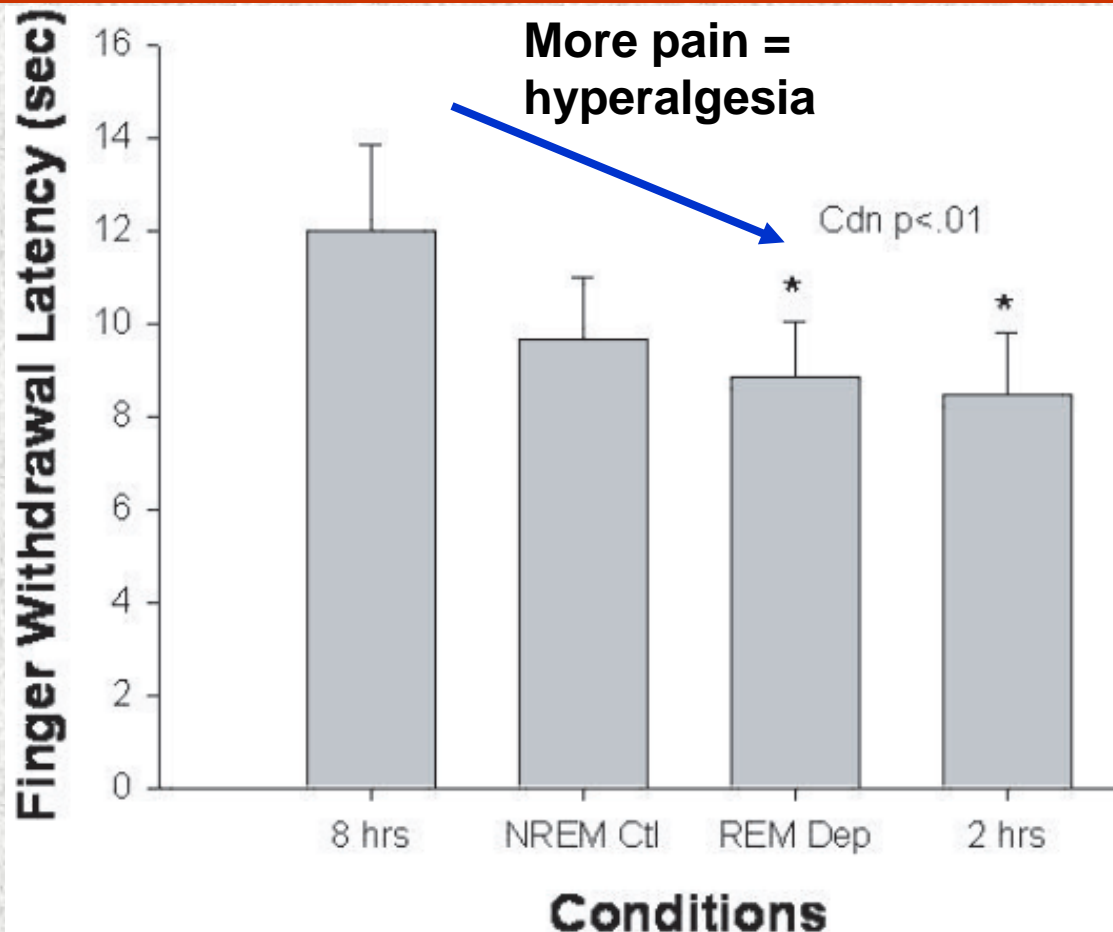


No specificity for REM deprivation - RESTRICTION

Both REM sleep stage deprivation and 2 hours of sleep restriction = **hyperalgesia**

lower mechanical pain threshold
(Normal male and female)

Threshold study =
first time heat or pressure
is perceive as painful



Roehrs et al, SLEEP 2006

EXPERIMENTAL TESTING during sleep

Common belief is that pain is due to poor deep sleep (St 3&4) quality Data derived from sleep deprivation with sound

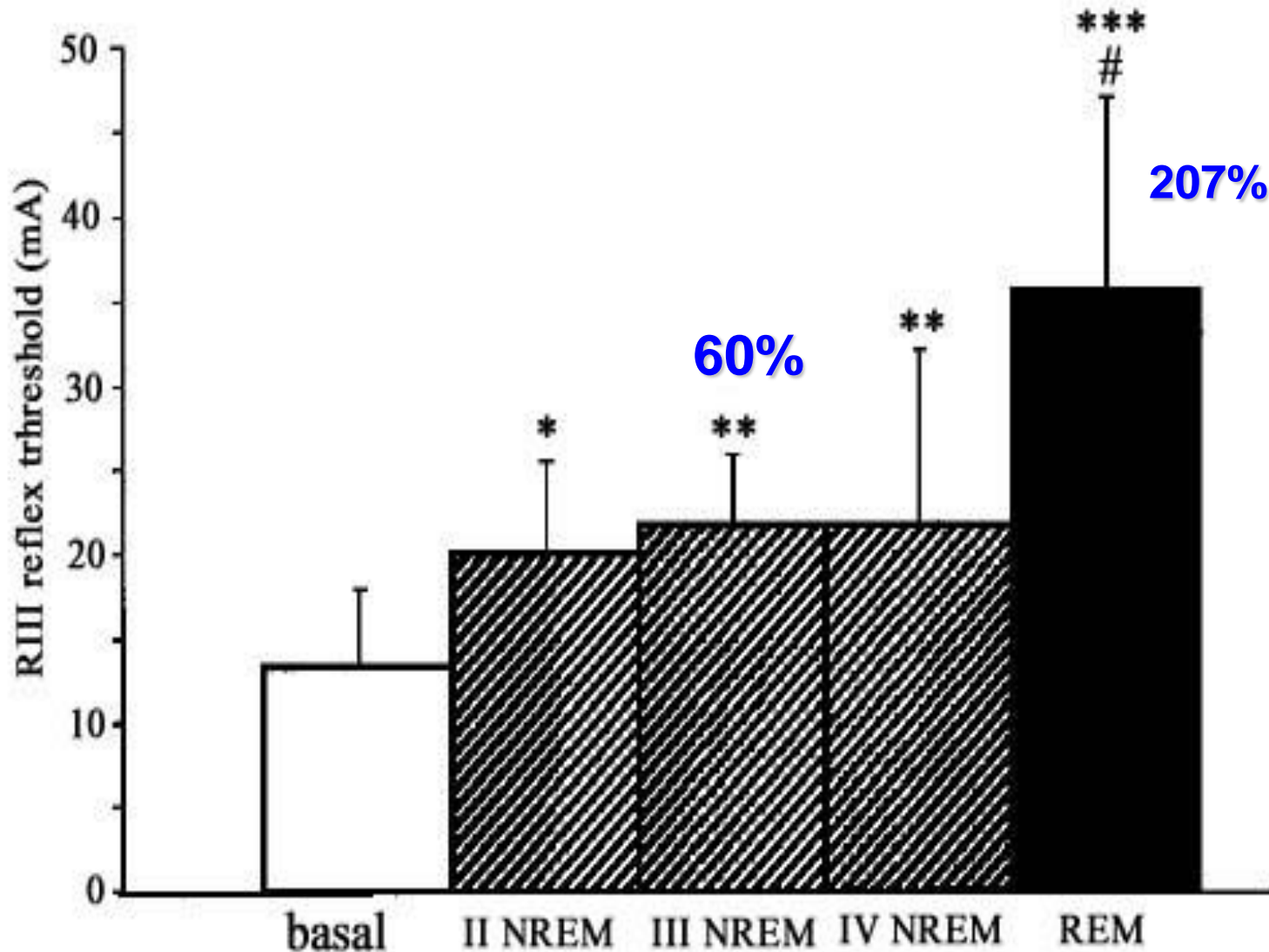
Sound > 65 db = awakening

- **St. 2 = higher responsiveness**
- **Deep sleep = low responsiveness**
- **REM = responsiveness related to
meaningfulness ¹**



Relevance to clinical pain ?

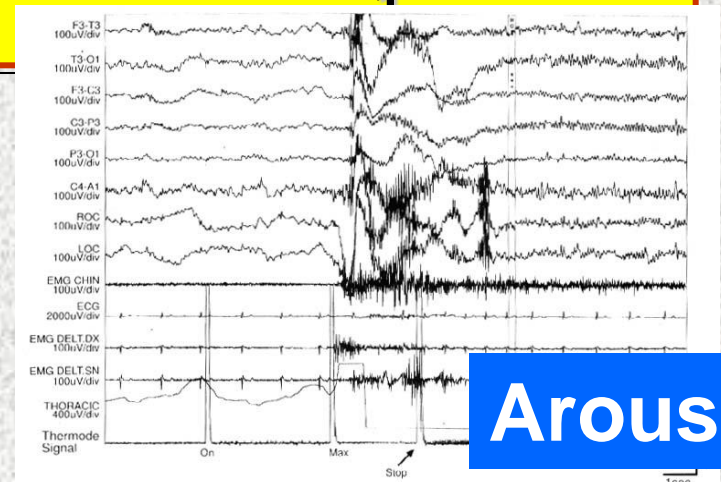
Human studies: Spinal nociceptive reflex threshold increased in REM sleep (electrical)



Mean of percentage of sleep-evoked arousal response by temperature and sleep stage for 8 subjects: About 50% response rate in Sleep Stage 2 and 30% in stages 3&4 or REM (*Lavigne, Pain 2000*)

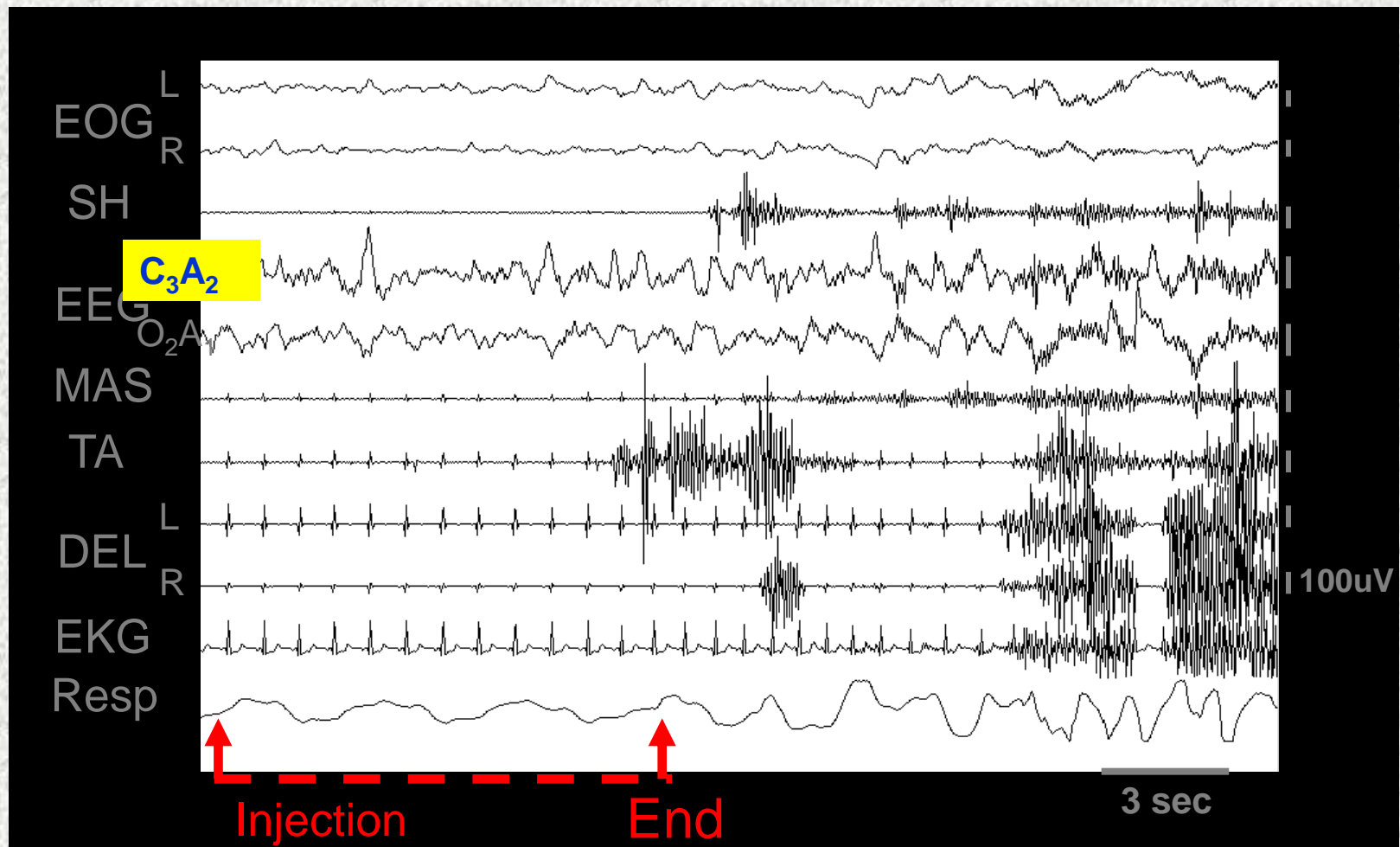
Sleep stage	CS (24°C)	WS (37°C)	HP (46-47°C)
2	33.4 ± 8.6	8.2 ± 2.7	48.3 ± 8.9
3&4	18.8 ± 8.6	1.2 ± 1.1	27.9 ± 5.3
REM	10.6 ± 4.0	4.7 ± 2.6	31.4 ± 9.0

Diagram illustrating the experimental design with temperature transitions: CS (24°C) → WS (37°C) → HP (46-47°C). Statistical significance is indicated by asterisks: ** for CS vs WS, *** for WS vs HP, and * for CS vs HP.



Arousal

Behavioral awakening response to hypertonic saline (5%) injection: **How to get closer to clinical pain related awakening during sleep**

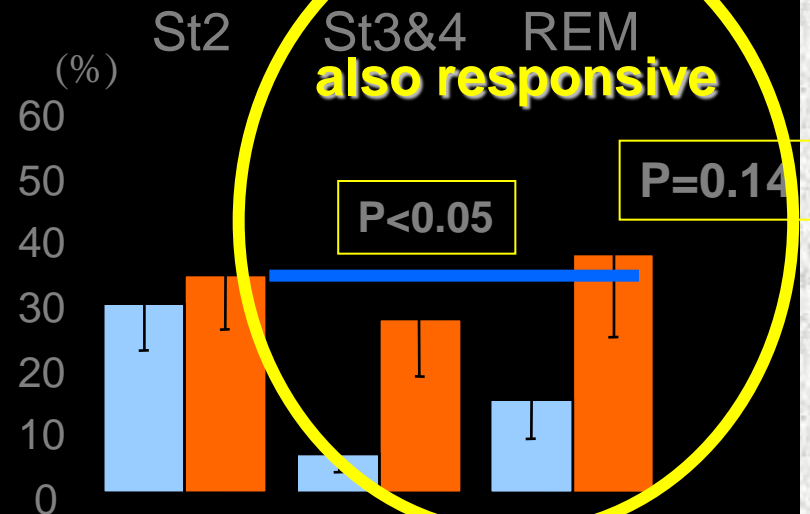


YES pain can be perceived during sleep period= arousal or awakenings

All sleep stages could be responsive to experimental pain if stimuli long enough to be processed: **Difference between non-pain (vibrotactile + auditory) and pain (hypertonic saline)**



B. Awakening (>10 sec)



(Vibrotactile + auditory) - (auditory)
 (Hypertonic) - (isotonic)

(mean ± SEM)

Management



The most frequent question from doctors after pain and sleep lectures:

**When does a sleep polygraphic recording is needed?
(ambulatory or sleep laboratory)**



WHEN:

- frequent sleepiness,
- persistent fatigue or NRS,
- transportation or work related accidents,
- sleep breathing disorders (snoring with sleepiness to apnea),
- periodic limb movements,
- sleep related headaches,
- etc

Step 1: Detection of a primary sleep disorder

(interview, questionnaire, polygraphic exam)

- **Insomnia,**
- **Sleep disordered breathing:**
Primary snoring to Apneas
- **Periodic Limb Movement (PLM),**
- **Headache & Bruxism, traumatic brain injury**
- **Daytime fatigue**
- **Daytime sleepiness = EPWORTH**
- **Circadian phase shift (habits, alcohol, trauma,etc)**
etc.

THE EPWORTH SLEEPINESS SCALE

(if more than 10/24 refer to MD)

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times.

Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

Available on Google

0 = no chance of dozing

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

SITUATION	CHANCE OF DOZING
Sitting and reading	_____
Watching TV	_____
Sitting inactive in a public place (e.g a theater or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

CUMULATIVE EFFECT of sub clinical comorbidities may have consequences on sleep continuity

**Increasing upper airway
collapsibility**

Breathing disorders continuum

- **Snoring**

TO

- **Upper airway resistance syndrome
(sleepiness mandatory)**

TO

- **Apneas (10 sec cessation) or
hypopneas**
- **& Obstructive Sleep Apnea (OSA)
syndrome**

**Treatment initiated at 10 RDI or AH/hr of
sleep**

CUMULATIVE EFFECT of sub clinical comorbidities may have consequences on sleep continuity

Periodic Limb (leg and arm) movements:

Clinical Cut Off is 10 PLM/hr of sleep

A concomitant condition that exacerbate sleep of pain patients



	Normal	Fibro/RA	PLMS
Index/h	2 (4.1)	8.8/ (10.8)	33

Okura 2008 for CWP-FM; Drewes 1998 for RA (data)

Prevalence of Symptoms post-Mild Traumatic Brain Injury (Chaput, Sleep Med 2009)

Self-reported Symptoms	10 Days Post-MTBI	6 Weeks Post-MTBI
Headaches	46.8%	39.9%
Dizziness	29.9%	
Forgetfulness	21.1%	RAPID ONSET
Fatigue		34%
Sleep complaints		33%
Impaired sleep due to pain	25.6%	14.8%
Frequent Awakenings	20.5%	34.8%
Increased sleep	10.3%	2.2%
Difficulty falling asleep	7.7%	9%
Impaired sleep due headaches	2.6%	
Nightmares	2.6%	

STEP 2: Evaluation of sleep hygiene

- **Sleep environment (e.g., dark, cool and quiet bedroom)**
- **Wake/sleep cycle (e.g., consistent bedtime and morning awakening)**
- **Life style habits (e.g., avoid intense exercise, smoking and/or alcohol at night)**
- **Presence of non sleeping infant, of a sick person to take care OR of a snoring or tooth grinding sleep partner – MANAGE schedule for sleep holidays!**
- **Excessive duration of day nap or evening nap habit (15-30 min max in PM not evening)**

Sleep hygiene advices

from Tang N and Smith M, Sleep Med for Dentists, Lavigne et al eds, Quintessence 2009

Box 24-1 Basic principles of sleep hygiene*

Maintain regular sleep-wake patterns and a consistent presleep routine (wind down)

- Arise at the same time each day (7 days a week), regardless of sleep quantity or quality the night before.
- Avoid extended naps to compensate for poor nighttime sleep (limit naps to 30 minutes).
- Eat regular meals and avoid heavy spicy foods for 2 hours prior to bed.
- Establish a relaxing bedtime ritual (discontinue stress-provoking activities well before bedtime).
- When unable to sleep, do not spend more than 15 to 20 minutes lying awake in bed. Get up and relax in separate room. Return to bed only when sleepy. Repeat this routine as often as necessary. This avoids establishing your room as a cue for alertness and distress.

Control environmental factors

- Ensure adequate light exposure in the morning and into the late evening.
- Take a 30-minute hot bath, 60 to 90 minutes before bedtime (not closer to bedtime).
- Set a wake-up alarm and keep the clock face turned away. Do not focus on how much time is spent awake in the middle of the night.
- Keep the sleeping environment dark, quiet, comfortable, and slightly on the cool side.
- Use a white noise machine to screen out background noise and decrease arousal threshold.

Sleep hygiene advices

from Tang N and Smith M, Sleep Med for Dentists, Lavigne et al eds, Quintessence 2009

Exercise

- Take regular exercise each day.
- Avoid vigorous exercise right before bed.

Limit stimulating substances and know drug effects

- Avoid smoking or nicotine several hours before bedtime and never smoke in the middle of the night.
- Limit the use of alcohol at night because it fragments sleep as it is metabolized.
- Reduced caffeine use and discontinue all caffeine 8 hours before bedtime (coffee, tea, soft drinks, chocolate, etc).
- Avoid over-the-counter sleep medication. Consult a sleep specialist about medication.
- Review the timing of all medications with your doctor, because they may negatively impact sleep and might be substituted or scheduled differently.
- Ensure adequate pain medication at night if needed.

*Adapted with permission from Smith and Haythornthwaite.³²



***Avoid opioids (morphine or codeine) at bedtime
if SLEEP Disorder Breathing***

STEP 3: Behavioural/Cognitive strategies & Physical management


- **Establish regular routines** for evening relaxation, avoid “bringing work home” and intense/troubling evening discussions, develop a **short nap schedule if possible during daytime** (≤ 20 min or 10-30 min based on rapidity to reverse grogginess)
- **Moist heat application** (10-20 min) or **ice massage** (5 min)
- **Physical manipulations: massage-fascia therapy, physical therapy – osteopathy, chiropractic; transcutaneous electrical nerve stimulation (TENS)**

Table 24-1**Individual treatment components of CBT-I***

Therapy	Content	Objectives	AASM level of recommendation ¹	Overlap with pain management ²
Stimulus control therapy	Instructing the patient to: (1) go to bed only when sleepy; (2) use the bedroom only for sleep and sex; (3) get out of bed if not asleep within 15 to 20 minutes; (4) maintain a regular sleep-wake schedule; and (5) avoid naps	To train the patient to reassociate the bed and bedroom with rapid sleep onset	Standard	No
Relaxation training	Techniques to reduce somatic or cognitive tension around bedtime	To deactivate the arousal system and facilitate sleep onset	Standard	Yes
Sleep restriction	Cutting the amount of time in bed down to the actual amount of time asleep	To increase sleep pressure and consolidate sleep by introducing a mild form of sleep deprivation	Guideline	No
Paradoxical intention	Instructing the patient to remain awake and avoid any effort or intention to fall asleep	To reduce sleep effort and performance anxiety that inhibits sleep onset	Guideline	No
Biofeedback	Providing visual or auditory feedback to patients to help increase their control over some biologic responses	To reduce somatic arousal and improve self-efficacy	Guideline	Yes

Tang and Smith, Sleep Med for Dentists, Quintessence 2009, Lavigne et al eds

Table 24-1**Individual treatment components of CBT-I***

Therapy	Content	Objectives	AASM level of recommendation [†]	Overlap with pain management [‡]
Cognitive therapy	Identifying and challenging patients' unhelpful cognitions about sleep and replacing them with more helpful substitutes through the flexible use of a range of discussion techniques	To alter unhelpful beliefs and attitudes about sleep and to reduce patients' emotional distress associated with sleep	No recommendation level	Yes, but focused on pain-related thoughts
Sleep hygiene education 	Teaching patients the potential impact of certain environmental, dietary, and behavioral factors on sleep	To increase awareness of environmental factors and health practices that may either promote or interfere with sleep	No recommendation level	No
Imagery training	Use of visualization techniques to focus patients' attention on pleasant or neutral images	To reduce presleep cognitive arousal or shift the focus of attention away from distressing, sleep-interfering thoughts	No recommendation level	Yes, but focused on pain-related imageries; for relaxation or distraction

SCIENTIFIC INVESTIGATIONS

Cognitive Behavioral Therapy for Insomnia Improves Sleep and Decreases Pain in Older Adults with Co-Morbid Insomnia and Osteoarthritis

Michael V. Vitiello, Ph.D.¹; Bruce Rybarczyk, Ph.D.²; Michael Von Korff, Ph.D.³; Edward J. Stepanski, Ph.D.⁴

MV Vitiello, B Rybarczyk, M Von Korff et al

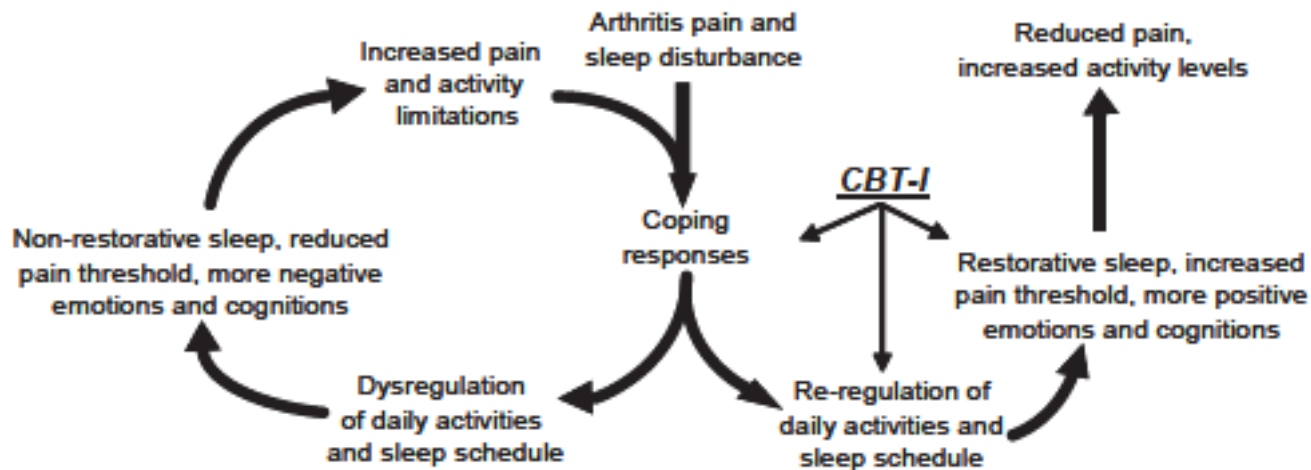


Figure 1—Conceptual model: Impact of cognitive behavioral therapy for insomnia (CBT-I).

**See also
Nicole Tang
papers:
CBT needs
to be
adapted to
pain and sleep
concomitant
complaints**

SUMMARY for MANAGEMENT - 1

Few therapeutic avenues may improve sleep of pain patients:

- Confirm if no sleep disorder... Apnea, insomnia, PLM...
- Cognitive & behavioural advices, CBT by psycho or nurse
- Medications and CAM:
 - **NSAI** with muscle relaxant (go with usual pain killer) or antihistamic (PM formula);
 - **trazodone** PRN or TCA Off label;
 - **pregabalin** (FDA, Health CDN for PAIN in FM; No in EC)

SUMMARY for MANAGEMENT- 2

Few therapeutic avenues may improve sleep of pain patients:

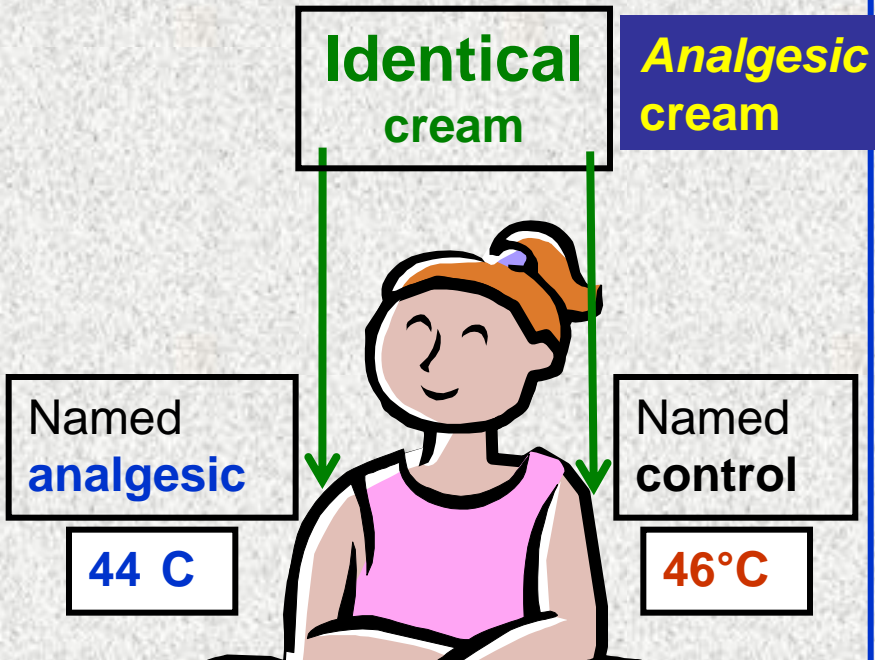
OR for short term: cyclobenzaprine, clonazepam, pramipexole (if **PLM**), sodium oxybate: **Off label**

- **Antidepressive/mood:** amitryptiline OR duloxetine, minalcipran (for PAIN in FM, OK from FDA)
- **CAM:** Cannabis related medication, melatonin, chamomile, etc (younger age...)
- **Respiratory devices:** CPAP, mandibular advancement oral appliance



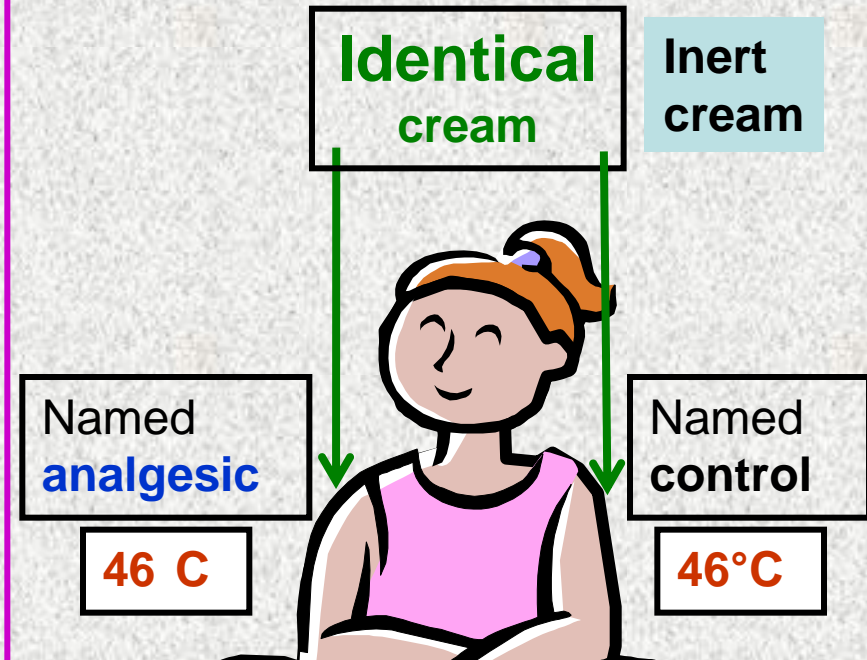
PLACEBO in SLEEP AND PAIN INTERACTION

PLACEBO Analgesia Conditioning:



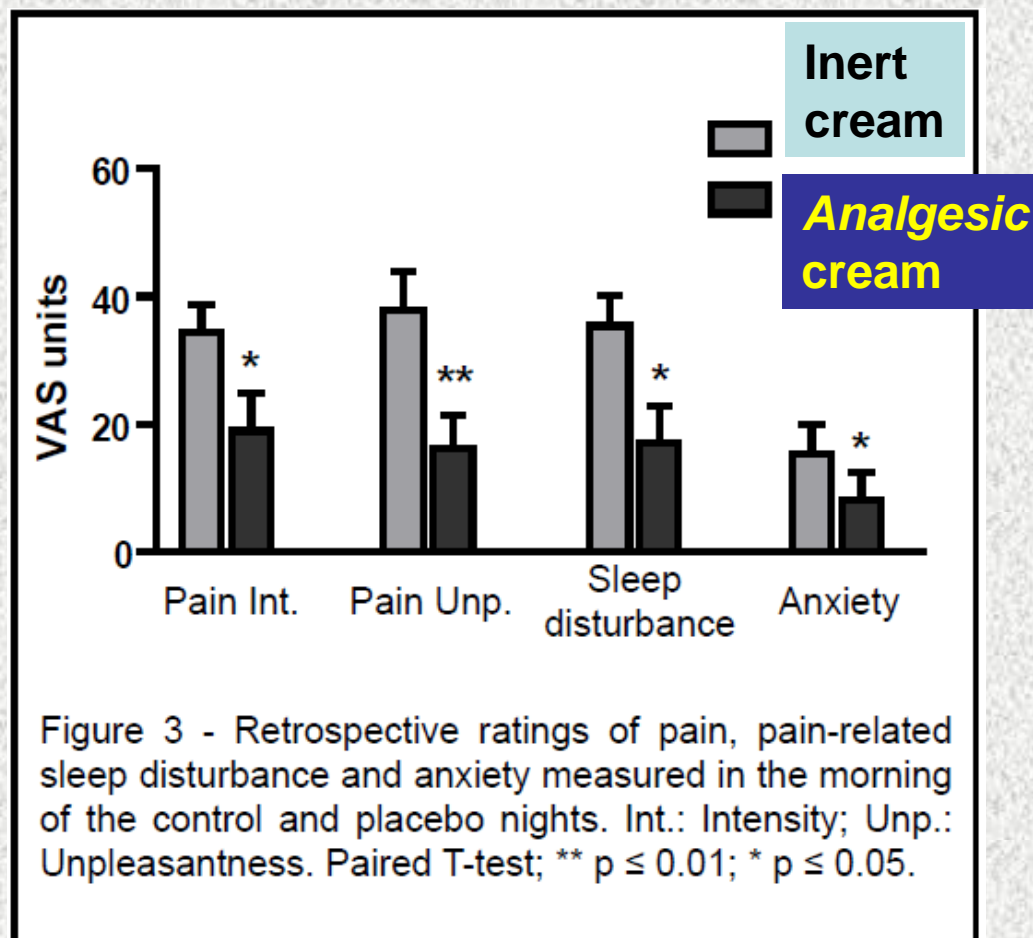
We said we applied the **same** thermal stimulus
But on the analgesic side, temperature set 2 C lower

PLACEBO Inert cream Testing:



we applied the **same** thermal stimulus

SELF REPORT on morning : **less pain, anxiety and sleep disruption** **under pre-sleep** **Placebo Analgesia Conditioning**



% arousal responses: Nociceptive stimulations and associated arousal responses (Percent are displayed in bracket)

+ response during Control night

Inert cream

random

Analgesic cream

+ response during Placebo Analgesia Conditioning night

1- During Inert Cream night: lower AROUSAL response rate in SWS (75%)

but higher in REM (93%)

Could this be a compensatory-protective mechanism? SWS is having a synaptic 'restoring' function (Tononi, J Clin Sleep Med 2009)

2- During Placebo Analgesia Conditioning night: higher AROUSAL response rate in Stage 3&4 - SWS (89%) but lower in REM (83%)

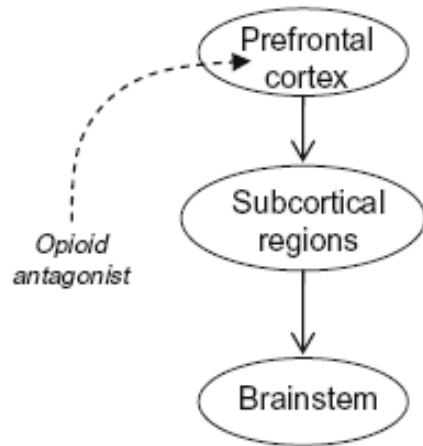
Could this reflects REM state promoting effect on expected analgesia? Modulation & integration of emotional events from WAKE to REM sleep (Vandekerckhove & Cluydts, Sleep Med Rev 2010)

SEE also the PARADOX: Frontal Cortex role in PAIN vs. SLEEP studies...

**Benedetti F,
PAIN 2010**

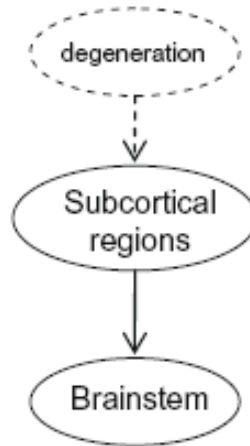
A

*Pharmacological
opioid blockade*



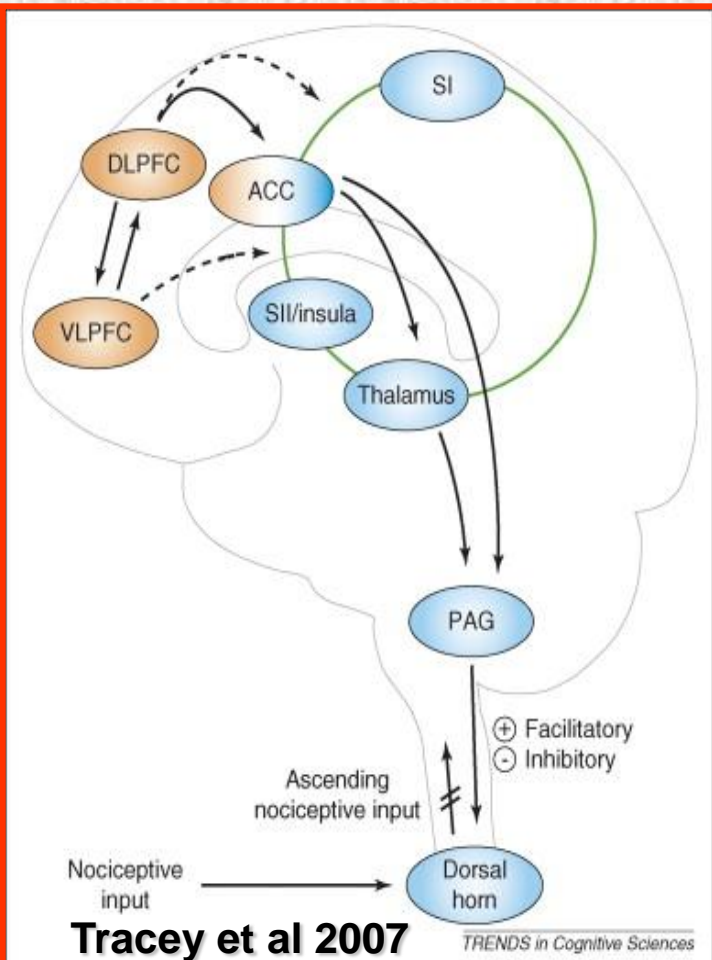
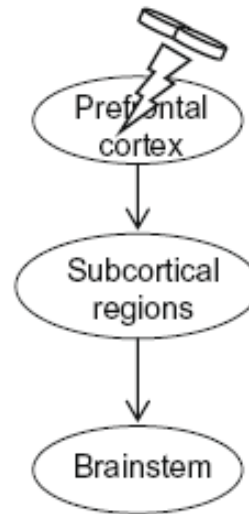
B

*Alzheimer's
disease*



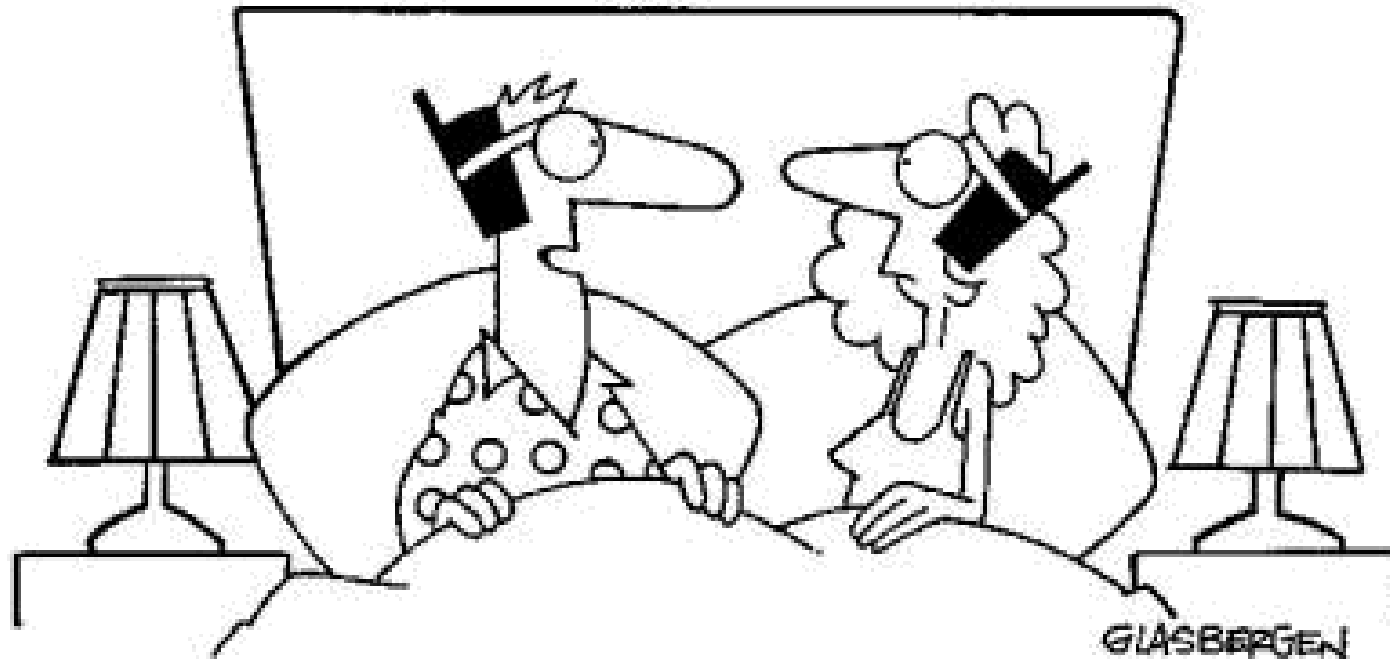
C

*Transcranial
magnetic
inactivation*



- **Pre-frontal Cortex** : Awake TOP DOWN Placebo Analgesia= Dorso Lat PFC= opioid vs. VLPFC= non opioid (Petrovic 2010)
- **PARADOX**: DLPFC deactivated during REM sleep (Maquet 1996, 2000; Vandekerckove 2010) = **Could placebo analgesia during sleep be non opioid?**

THANK YOU



**“With wireless sleep technology, the people
in my dreams can send e-mail and faxes
to the people in your dreams!”**

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phone: (216) 371-8600 / e-mail: ft@funnytimes.com

Alpha-delta sleep (fast/slow EEG wave) : is not specific to pain, not a biomarker and not pathognomonic

- Present in FM, OA and also in sleep apnea, bruxism, periodic limb movement patients and during sleep of **normal/healthy subjects** if sleep occur in a milieu with noise (e.g., an hotel, a plane (90 dB)), etc
- Difference found in **Fibromyalgia patients** (Moldofsky 1975; Drewes 1995 FM; 1998 OA) was marginal and may reflect changes in **cognitive function (Frontal EEG), higher frequency of limb movement**, etc (see reviews : Mahowald 2000; Dauvilliers IASP 2007; Chervin 2009)
- **Shorter sleep stage 2 duration predict** higher pain scores and current pain intensity in FM patients (Burns 2008)

Table 24-1**Individual treatment components of cognitive behavior therapy for insomnia (CBT-I)***

Therapy	Content	Objectives	AASM level of recommendation†	Overlap with pain management‡
Stimulus control therapy	Instructing the patient to: (1) go to bed only when sleepy; (2) use the bedroom only for sleep and sex; (3) get out of bed if not asleep within 15 to 20 minutes; (4) maintain a regular sleep-wake schedule; (5) and avoid naps	To train the patient to reassociate the bed and bedroom with rapid sleep onset	Standard	No
Relaxation training	Techniques to reduce somatic or cognitive tension around bedtime	To deactivate the arousal system and facilitate sleep onset	Standard	Yes
Sleep restriction	Cutting the amount of time in bed down to the actual amount of time asleep	To increase sleep pressure and consolidate sleep by introducing a mild form of sleep deprivation	Guideline	No
Paradoxical intention	Instructing the patient to remain awake and avoid any effort or intention to fall asleep	To reduce sleep effort and performance anxiety that inhibits sleep onset	Guideline	No
Biofeedback	Providing visual or auditory feedback to patients to help increase their control over some biologic responses	To reduce somatic arousal and improve self-efficacy	Guideline	Yes

Tang and Smith, Sleep Med for Dentists, Quintessence 2009, Lavigne et al eds

Table 24-1

Individual treatment components of cognitive behavior therapy for insomnia (CBT-I)*

Therapy	Content	Objectives	AASM level of recommendation†	Overlap with pain management‡
Cognitive therapy	Identifying and challenging patients' unhelpful cognitions about sleep and replacing them with more helpful substitutes, through the flexible use of a range of discussion techniques	To alter unhelpful beliefs and attitudes about sleep and to reduce patients' emotional distress associated with sleep	No recommendation level	Yes, but focused on pain-related thoughts
Sleep hygiene education	Teaching patients the potential beneficial or detrimental impact of certain environmental, dietary, and behavioral factors on sleep	To increase awareness of environmental factors and health practices that may either promote or interfere with sleep	No recommendation level	No
Imagery training	Use of visualization techniques to focus patients' attention on pleasant or neutral images	To reduce presleep cognitive arousal or shift the focus of attention away from distressing, sleep-interfering thoughts	No recommendation level	Yes, but focused on pain-related imagery; for relaxation or distraction