



## 4<sup>e</sup> Symposium Séduno-Fribourgeois de Médecine Intensive

# Troubles du sommeil aux soins intensifs: Impact et prise en charge

**Dr Nawfel Ben Hamouda MD, MSc**  
Médecin associé, MER



**11.11.2022**

# Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU



Devlin JW, et al. Crit Care Med 2018

# Fréquents ?

Soif 63%

Anxiété/Peur 62%

Manque de  
sommeil 61%

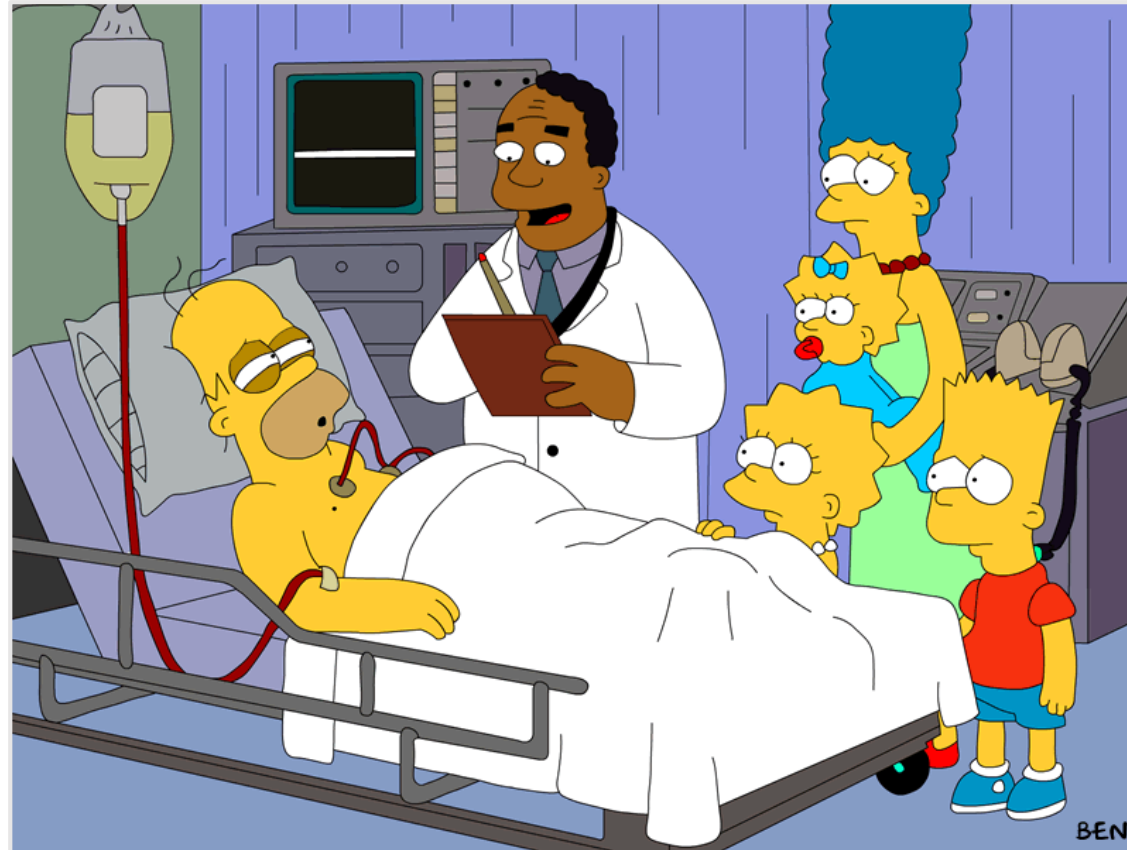
Solitude  
Isolement 46%

Douleur 43%

Chaud/Froid  
28/37%

Faim 13%

## Ressenti des patients ?



USI, n= 76  
med, chir, trauma

LOS 4.4 J

*Simini B. Lancet 1999*

# Caractéristiques ?

## Première nuit postop

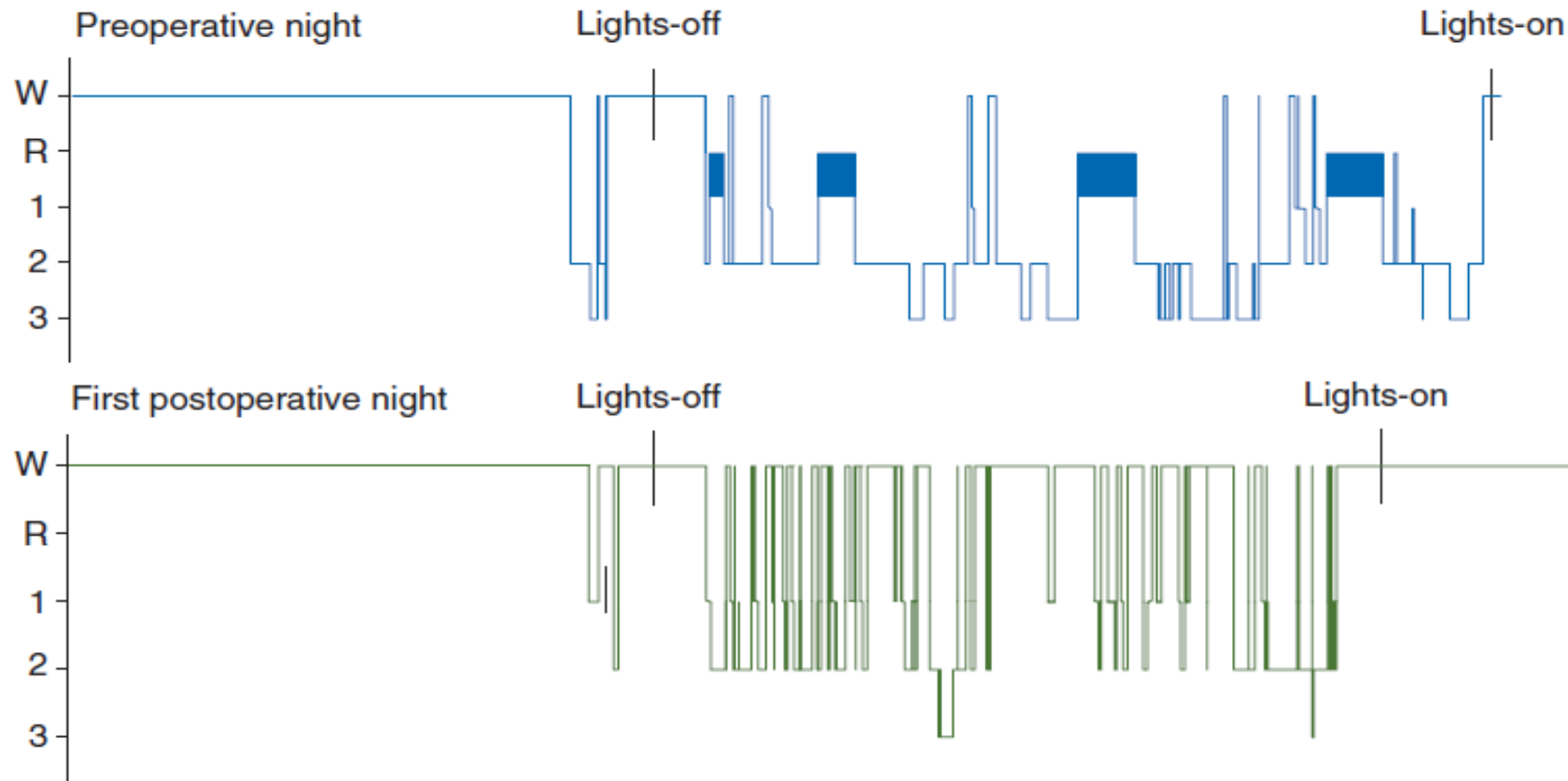
British Journal of Anaesthesia 109 (5): 769–75 (2012)  
Advance Access publication 24 July 2012 · doi:10.1093/bja/aes252

BJA

### NEUROSCIENCES AND NEUROANAESTHESIA

#### Sleep disturbances after fast-track hip and knee arthroplasty

L. Krenk<sup>1,2\*</sup>, P. Jennum<sup>3</sup> and H. Kehlet<sup>1,2</sup>



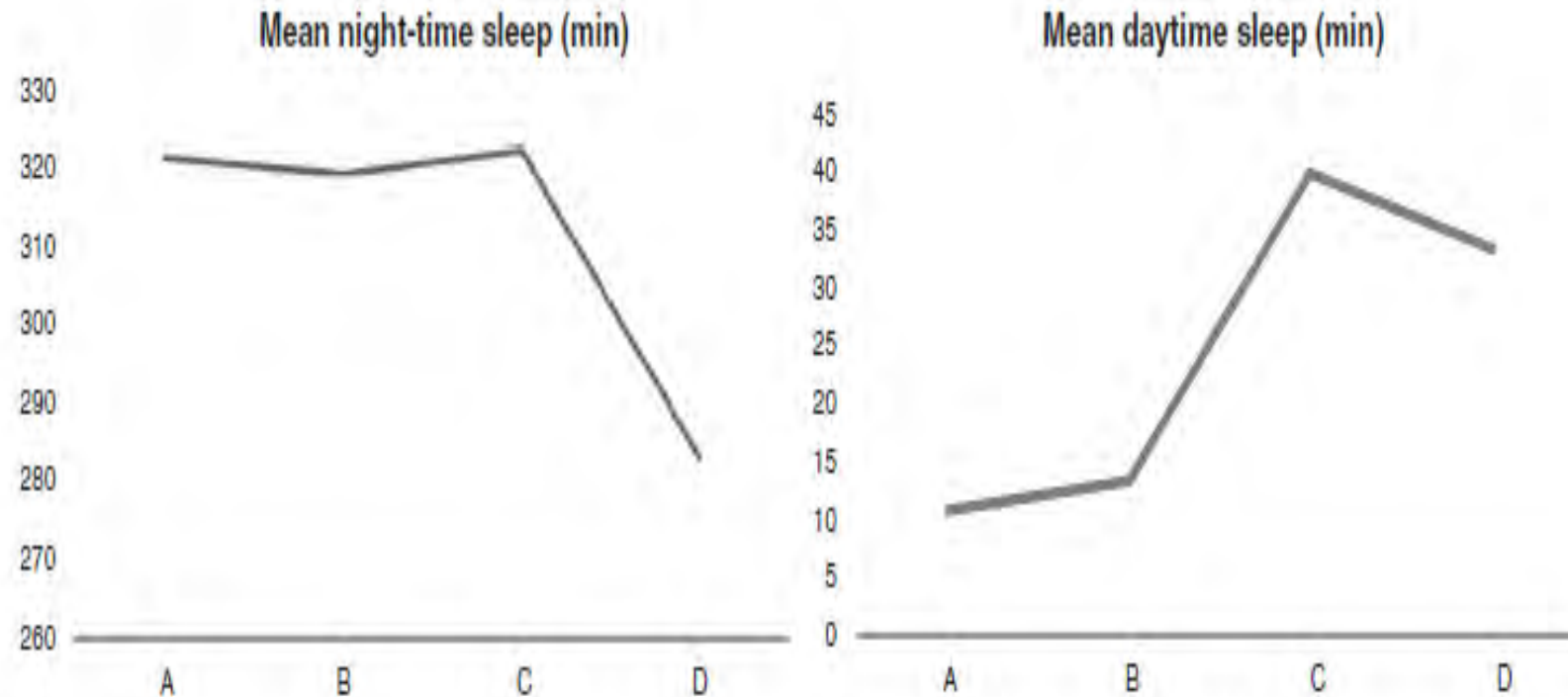
**Krenk et al. Br J Anaesth 2012**

# Caractéristiques ?

## Activity, Sleep and Cognition After Fast-Track Hip or Knee Arthroplasty

Lene Krenk, MD<sup>a,b,c</sup>, Poul Jennum, PhD<sup>d</sup>, Henrik Kehlet, PhD<sup>a,b</sup>

## Nuits postopératoires



**Fig. 2.** Development of activity, pain and sleep parameters according to time periods; preoperatively (A), during hospitalisation (B), about 4 days postoperatively at home (C), about 6 days postoperatively at home (D).

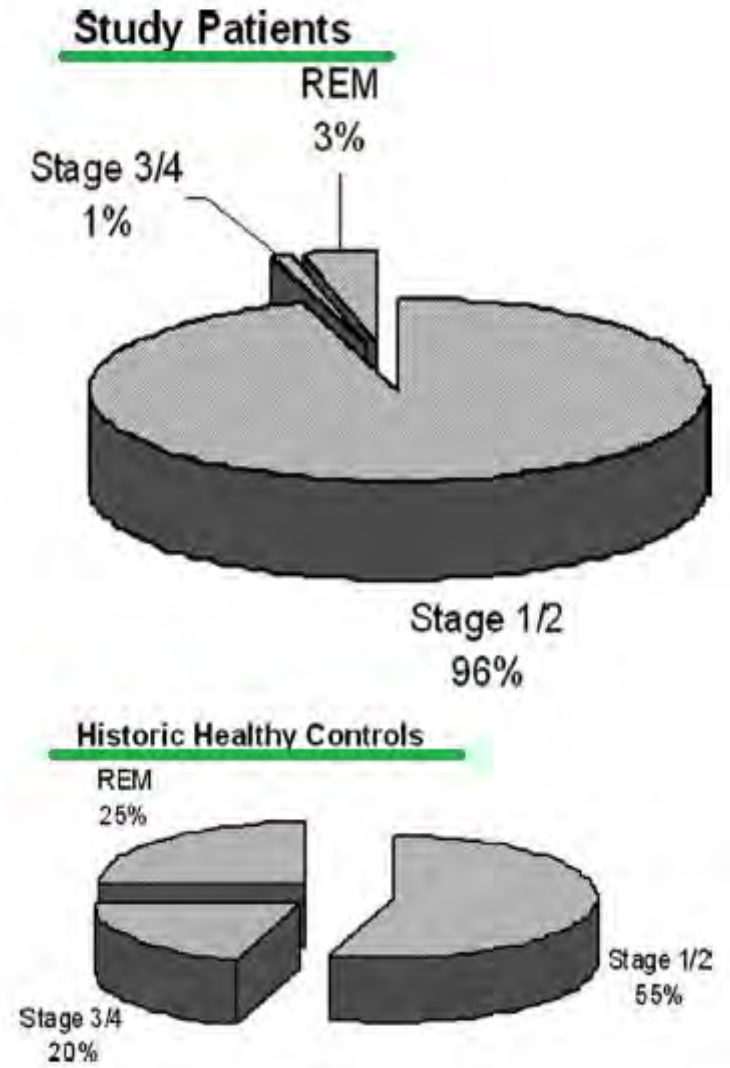
***Krenk et al. J Arthroplasty 2013***

# Caractéristiques ?

## Quantity and Quality of Sleep in the Surgical Intensive Care Unit: Are Our Patients Sleeping?

Randall S. Frieze, MD, Ramon Diaz-Arrastia, MD, PhD, Dara McBride, RN, Heidi Frankel, MD, and Larry M. Gentilello, MD

Variable	Median [IQR]/Count	Range/Proportion
Age (yr)	37.5 [31, 58.3]	20–83
Male	13	81.3%
Trauma	10	62.5%
Mechanical ventilation	5	31.3%
ICU day at PSG	3 [2, 9.5]	2–19
Patients receiving narcotic during PSG recording	13	81.3%
Patients receiving benzodiazepam during PSG recording	3	18.8%



*Frieze et al. J Trauma 2007*

# Caractéristiques: Résumé

**Sommeil très fragmenté**

**Nombre de réveils**



**Temps total de sommeil**

= ou ↓

**NREM stade 1**



**NREM stade 2**

↓ ou ↑

**NREM stade 3**



**NREM Stade 4**



**REM**



*Friese. Crit Care Med 2008*

*Weinhouse et al. Sleep 2006*

# Conséquences?

***Kerr RG, et al. Am J Crit Care 2016***

# Conséquences: complications postopératoires

## Does Sleep Quality Affects the Immediate Clinical Outcome in Patients Undergoing Coronary Artery Bypass Grafting: A Clinico-biochemical Correlation

Table 2: Comparison of demographics and clinical profile of patients in both the groups by Chi-square test

Parameters	Group I, PSQI $\leq 5$ (n=101)	Group II, PSQI $> 5$ (n=55)	P
Duration of mechanical ventilation (h)	10.10 $\pm$ 8.19	14.76 $\pm$ 12.05	0.001
Duration of ICU stay (days)	2.08 $\pm$ 0.95	2.70 $\pm$ 1.45	0.0016
Postoperative complication (yes) <sup>†</sup>	3 (2.9)	24 (43.43)	0.0001

Table

associated with a higher incidence of adverse perioperative events in patients undergoing elective CABG.

**Conclusion:** Poor sleep quality

t,

Parameters	PSQI $\leq 5$ (n=101)	PSQI $> 5$ (n=55)	P
Arrhythmia	7 (6.93)	16 (29.09)	0.001
Respiratory dysfunction	0	4 (7.2)	0.007
Infection	3 (2.9)	4 (7.2)	0.220
Myocardial dysfunction and low cardiac output syndrome	0	2 (3.63)	0.056
Neurological complication	0	1 (1.81)	0.17
Renal dysfunction	0	4 (7.2)	0.006
Death	0	2 (3.63)	0.05

# Conséquences: Système immunitaire

## Partial night sleep deprivation reduces natural killer and cellular immune responses in humans

MICHAEL IRWIN,<sup>1</sup> JOHN MCCLINTICK, CAROLYN COSTLOW, MELISSA FORTNER, JACK WHITE, AND J. CHRISTIAN GILLIN

Departments of Psychiatry, University of California, and San Diego Veterans Affairs Medical Center, San Diego, California 92161, USA

42 volontaires  
sains  
22h→3h

## Effects of 48 Hours Sleep Deprivation on Human Immune Profile

Levent Öztürk<sup>1</sup>, Zerrin Pelin<sup>2</sup>, Derya Karadeniz<sup>2</sup>, Hakan Kaynak<sup>2</sup>, Lütfi Çakar<sup>1</sup> and Erbil Gözükırmızı<sup>2</sup>

10 volontaires sains privés  
de sommeil x 48h  
vs 6 contrôles

Changes in NK cells (%)

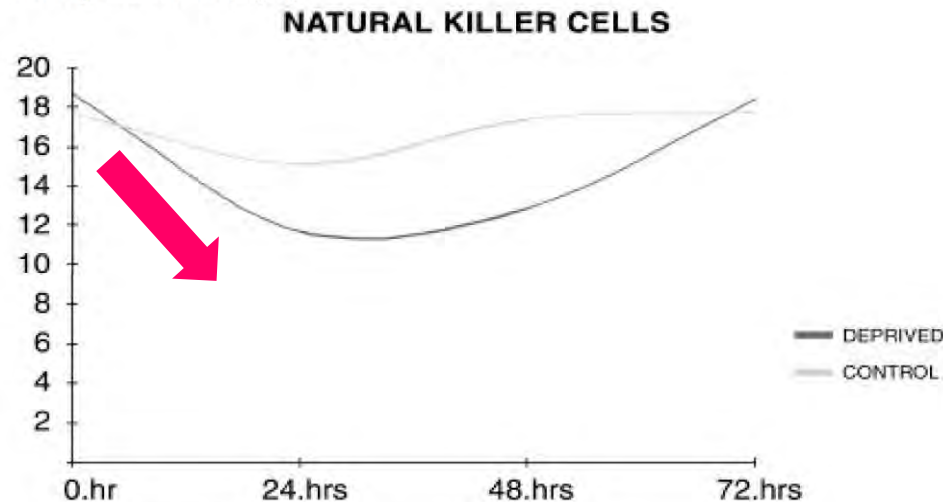
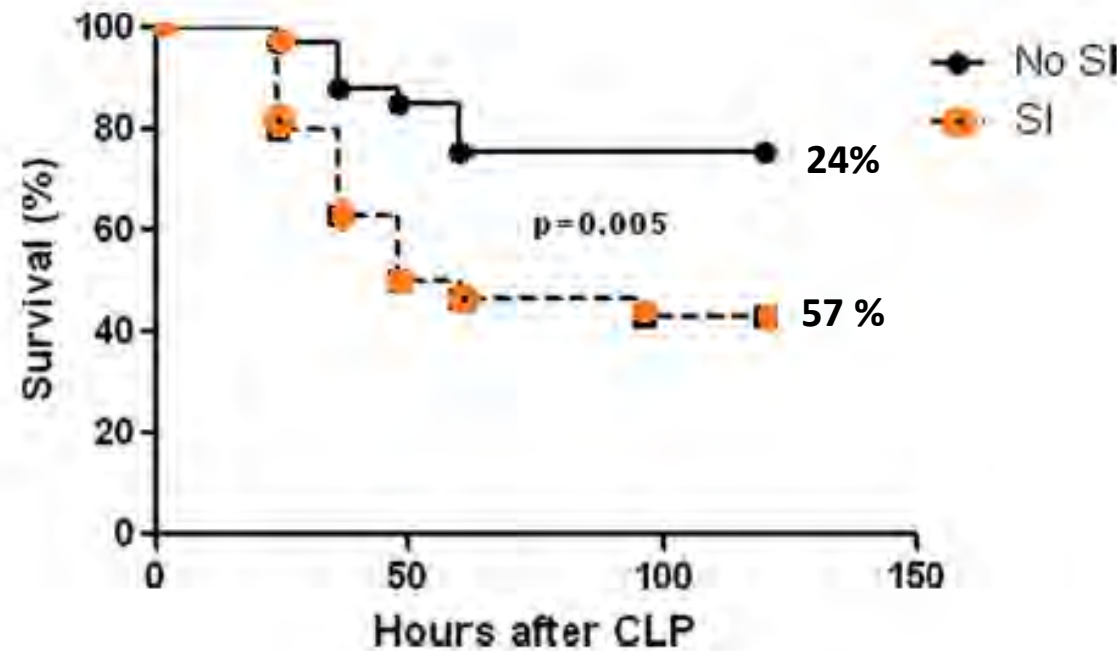


Figure 1. NK Cell Proportion in Sleep-Deprived and Control Subjects

*Irwin M, et al. FASEB J 1996*  
*Oztürk L, et al. Sleep Res Online 1999*

## Sleep Deprivation After Septic Insult Increases Mortality Independent of Age

*Randall S. Friese, MD, Brandon Bruns, MD, and Christopher M. Sinton, PhD*

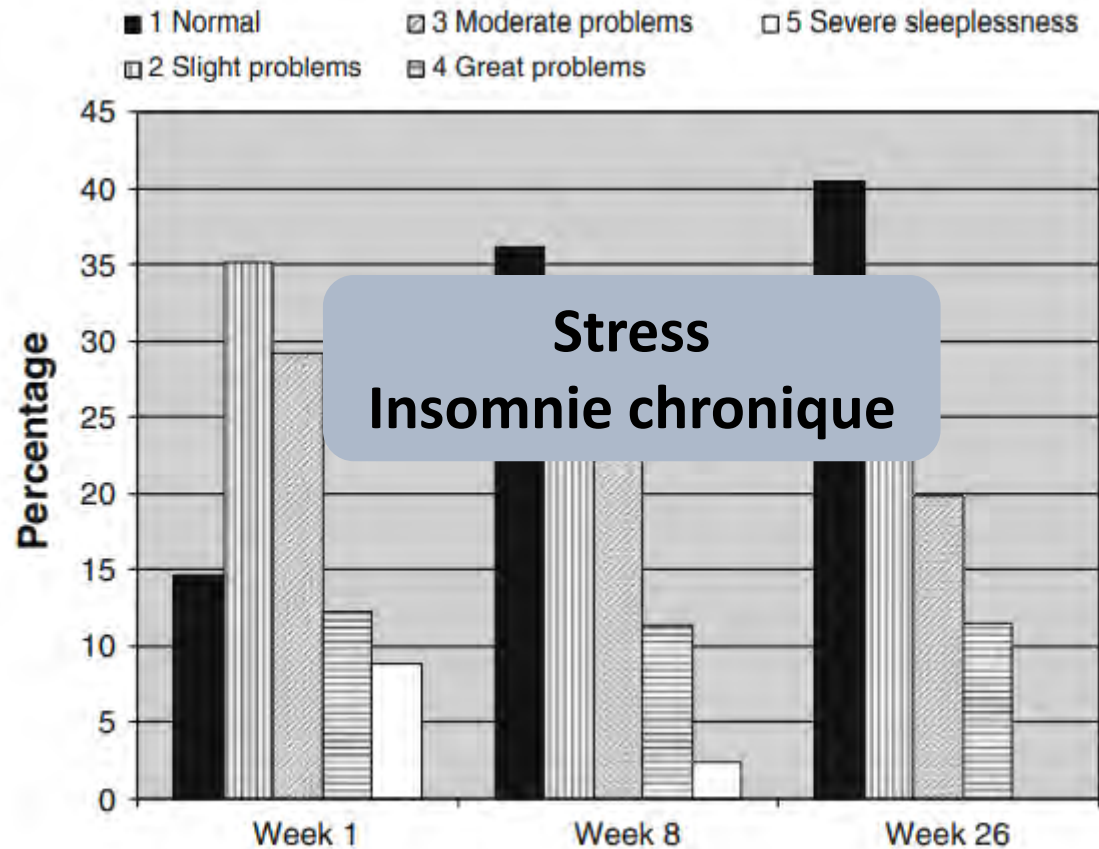


5-day survival curve after CLP with and without Sleep interruption x 48H

*Friese et al. J Trauma 2009*

# Conséquences: psychologiques

**Sleep and other factors associated with mental health and psychological distress after intensive care for critical illness**



**Fig. 2** Sleep problems reported at weeks 1, 8 and 26 after hospital discharge

**6 months ICU discharge**  
**LOS 48h, MV > 24h**  
**n = 195**  
**HRQOL**

Female gender, younger age and sleeping problems were associated with impaired psychological outcomes

**McKinley S, et al. Intensive Care Med 2012**

# Facteurs favorisants :

Lumière

Bruit

Ventilation

Sédation

Age

ATCDs

Douleur

Inflammation

Stress



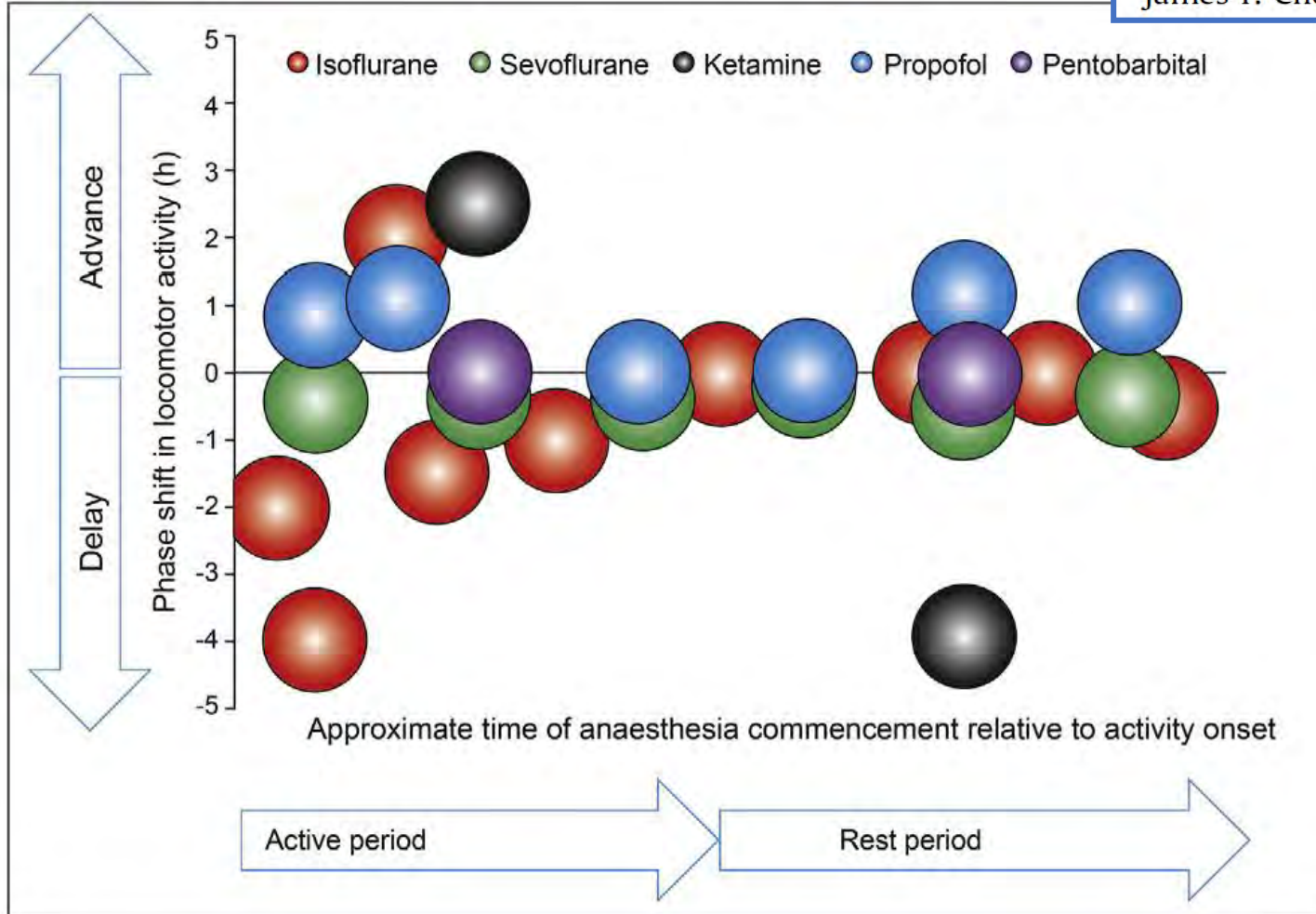
[www.theage.com.au](http://www.theage.com.au)

# Facteurs favorisants: les hypnotiques

## CLINICAL REVIEW

How does general anaesthesia affect the circadian clock?

Raewyn C. Poulsen<sup>a</sup>, Guy R. Warman<sup>b</sup>, Jamie Sleight<sup>c</sup>, Nicola M. Ludin<sup>b</sup>,  
James F. Cheeseman<sup>b, \*</sup>



*Poulsen RC, et al. Sleep Med Rev 2016*

# Facteurs favorisants: les hypnotiques

## Desynchronization of Daily Rest–Activity Rhythm in the Days Following Light Propofol Anesthesia for Colonoscopy

G Dispersyn<sup>1–3</sup>, Y Touitou<sup>1</sup>, O Coste<sup>2</sup>, L Jouffroy<sup>4</sup>, JC Lléu<sup>4</sup>, E Challet<sup>5</sup> and L Pain<sup>3</sup>

**Table 1** Diurnal and nocturnal rest duration as assessed by actigraphy during the reference period (mean value of 2 days), the day of light propofol anesthesia, and the 2 days following light propofol anesthesia ( $n = 17$ )



	Light propofol anesthesia			
	Reference period (24 h)	Day 0 (18 h)	Day 1 (24 h)	Day 2 (24 h)
Nocturnal rest	07:43 (41)	07:47 (74)	07:53 (57)	07:31 (49)
Diurnal rest	00:37 (32)	02:48 (70)*	01:13 (86)*	00:25 (49)

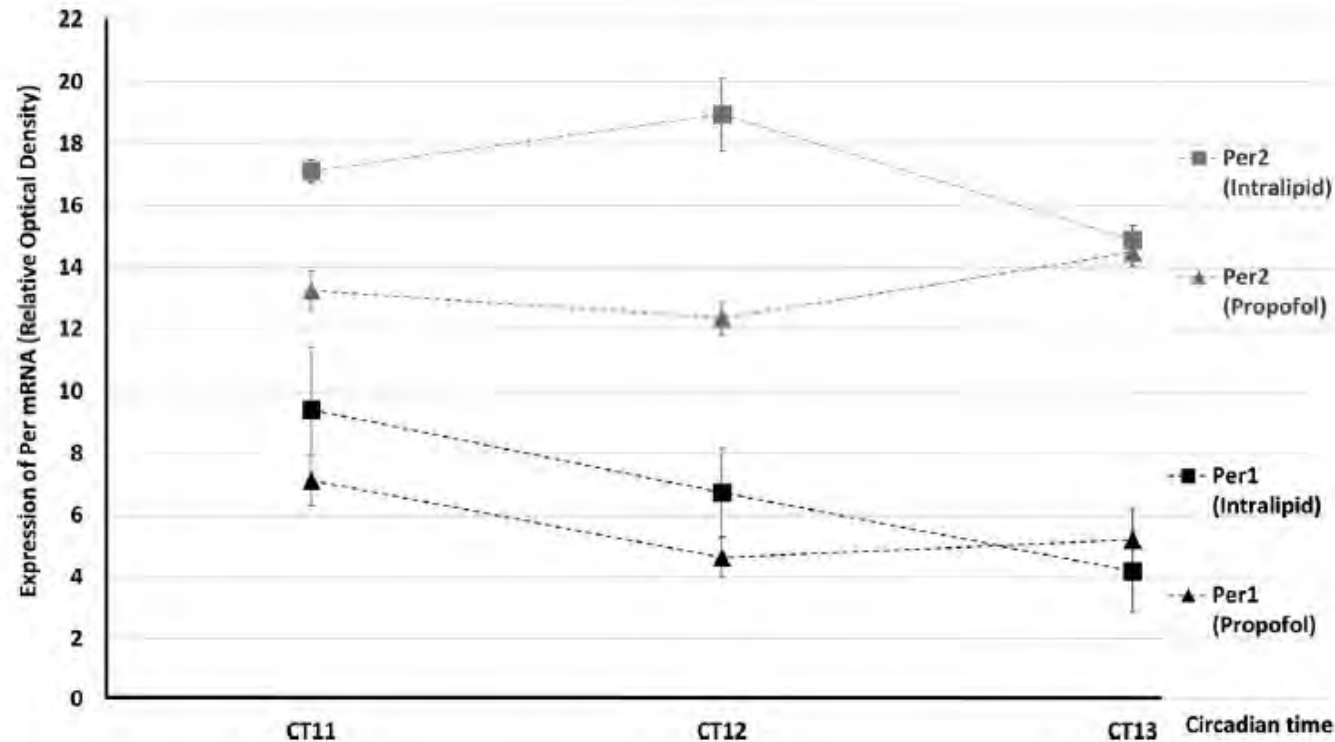
Mean values are expressed as hours:minutes, SD as minutes.

\*Value statistically different from the value for the reference period.

***Dispersyn et al. Clin Pharmacol Ther 2009***

## Short-term propofol anaesthesia down-regulates clock genes expression in the master clock

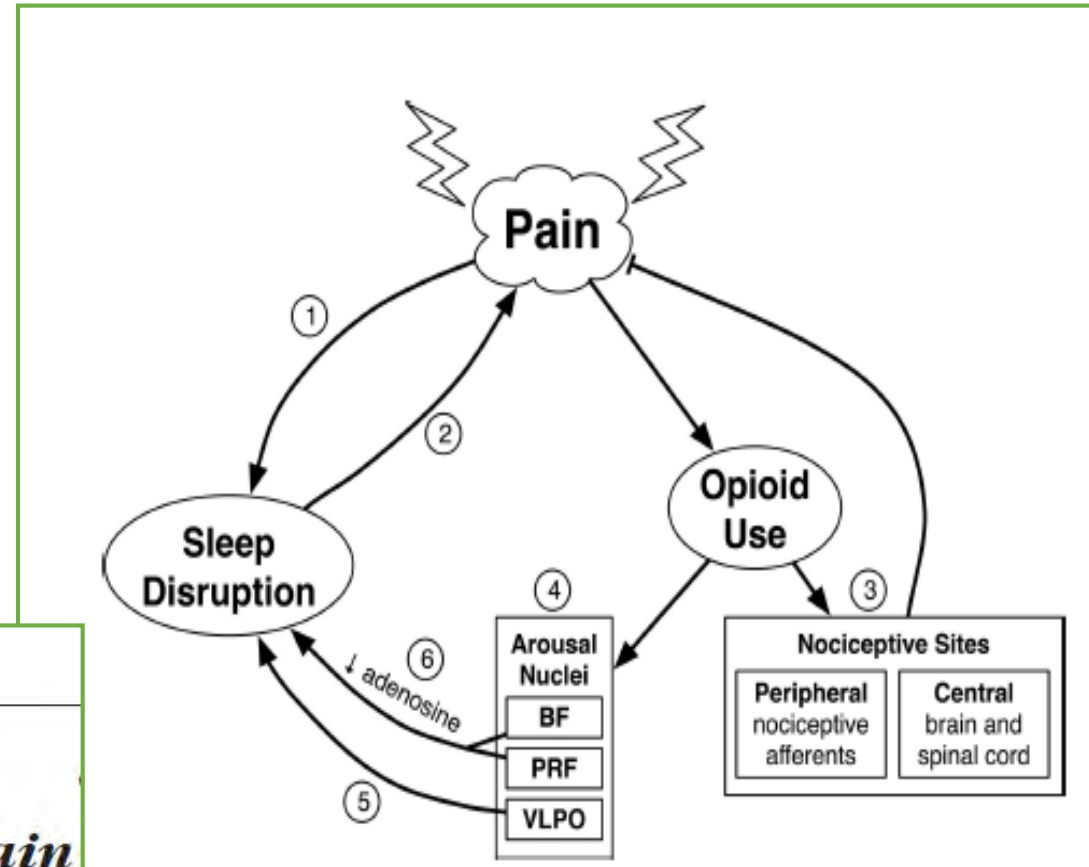
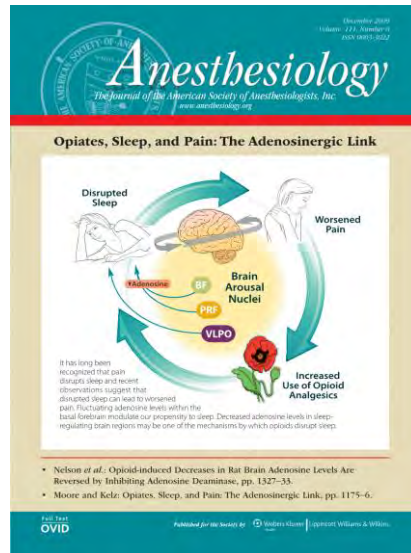
Nawfel Ben-Hamouda <sup>a,b</sup>, Vincent-Joseph Poirel<sup>a</sup>, Garance Dispersyn<sup>a,c</sup>, Paul Pévet<sup>a</sup>, Etienne Challet <sup>a</sup>,  
and Laure Pain<sup>a,d</sup>



**Figure 1.** Effect of propofol anaesthesia on the expression of Per1 and Per2 mRNA in the SCN of rats at different circadian times. For Per1: propofol group n=15, Intralipid® group n=12. For Per2: propofol group n=14, Intralipid® group n=12).

*Ben-Hamouda N, et al. Chronobiol Int 2018*

# Facteurs favorisant: les opiacés



## EDITORIAL VIEWS

Anesthesiology 2009; 111:1175-6

## Opiates, Sleep, and Pain

### The Adenosinergic Link

Moore JT, Kelz MB. Anesthesiology 2009

# Facteurs favorisants: autres médicaments

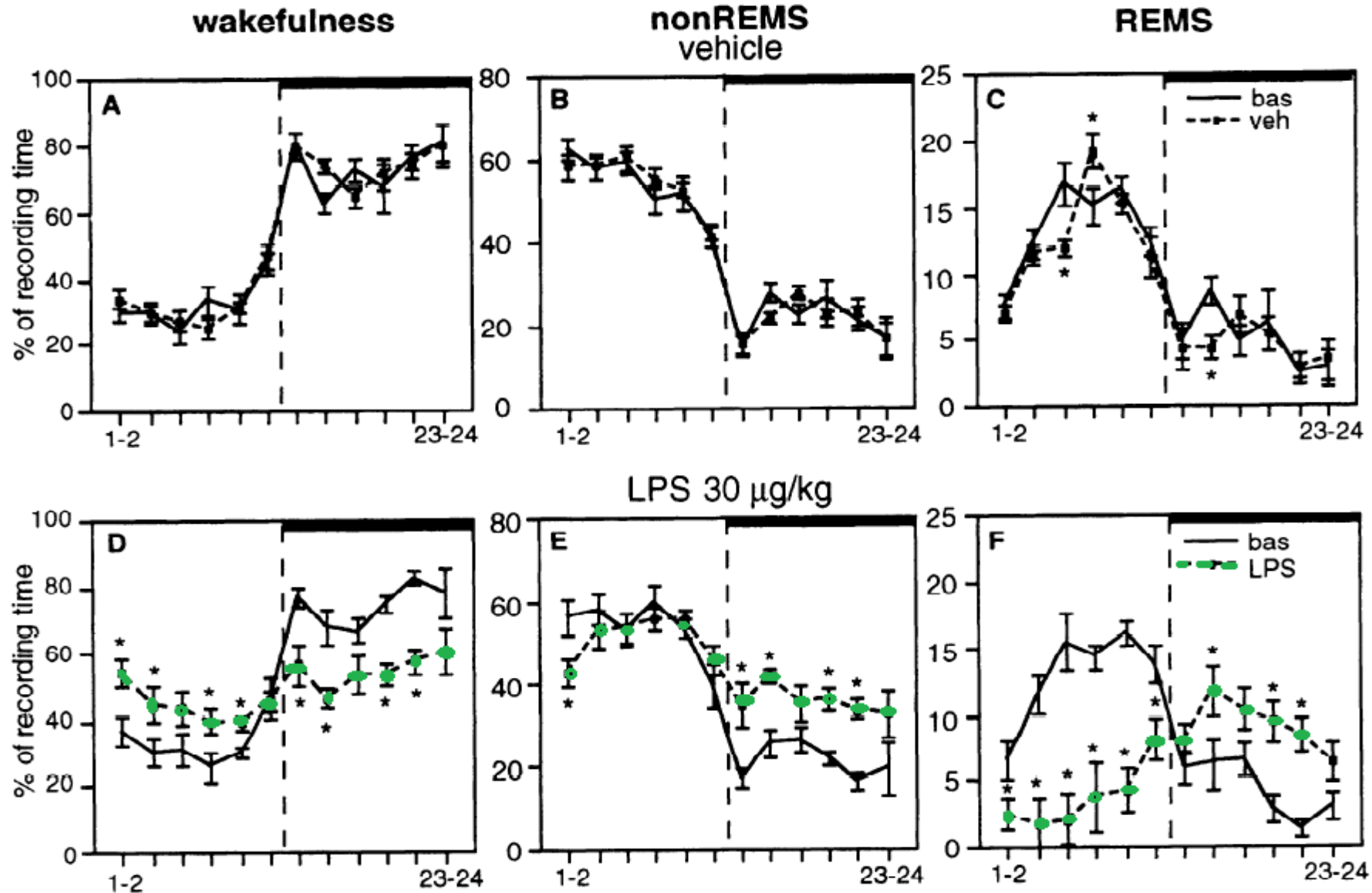
Drugs commonly used in ICU and their effects on sleep pattern.

Drug Class or Individual Drug	Sleep Disorder Induced or Reported	Possible Mechanism
Benzodiazepines	↓ REM, ↓ SWS	Gamma aminobutyric acid type A receptor stimulation
Opioids	↓ REM, ↓ SWS	μ receptor stimulation
Clonidine	↓ REM	α <sub>2</sub> receptor stimulation
Non steroidal anti-inflammatory drugs	↓ TST, ↓ SE	Prostaglandin synthesis inhibition
Norepinephrine/Epinephrine	Insomnia, ↓ REM, ↓ SWS	α <sub>1</sub> receptor stimulation
Dopamine	Insomnia, ↓ REM, ↓ SWS	D <sub>2</sub> receptor stimulation/α <sub>1</sub> receptor stimulation
β-Blockers	Insomnia, ↓ REM, Nightmares	Central nervous system β-blockade by lipophilic agents
Amiodarone	Nightmares	Unknown mechanism
Corticosteroids	Insomnia, ↓ REM, ↓ SWS	Reduced melatonin secretion
Aminophylline	Insomnia, ↓ REM, ↓ SWS, ↓ TST, ↓ SE	Adenosine receptor antagonism
Quinolones	Insomnia	Gamma aminobutyric acid type A receptor inhibition
Tricyclic antidepressants	↓ REM	Antimuscarinic activity and α <sub>1</sub> receptor stimulation
Selective serotonin reuptake inhibitors	↓ REM, ↓ TST, ↓ SE	Increased serotonergic activity
Phenytoin	↑ Sleep Fragmentation	Inhibition of neuronal calcium influx
Phenobarbital	↓ REM	Increased gamma aminobutyric acid type A activity
Carbamazepine	↓ REM	Adenosine receptor stimulation and/or serotonergic activity

REM, rapid eye movement; SWS, slow wave sleep; TST, total sleep time; SE, sleep efficiency.

***Bourne et al. Anaesthesia 2004***

# Facteurs favorisant: le sepsis



Effet de l'injection de LPS

# Facteurs favorisants: la ventilation mécanique

Patient, N	Stage 1, %	Stage 2, %	Stage 3 and 4, mins	Rapid Eye Movement, %	Fragmentation Index
1	2	83	102	1	15
2	1	64	119	18	25
3	5	57	246	10	35
4	8	68	73	0	41
5	10	66	98	7	41
6	7	64	67	13	53
7	8	48	91	7	37
8	1	51	178	13	67
9	17	49	63	15	20
10	10	47	119	12	19
11	4	49	300	11	29
12	3	88	54	0	11
13	15	41	151	11	51
14	16	74	31	5	14
15	8	79	35	2	23
Median [25–75th percentiles]	8 [3–11]	63 [48–74]	98 [63–151]	10 [2–13]	29 [19–41]

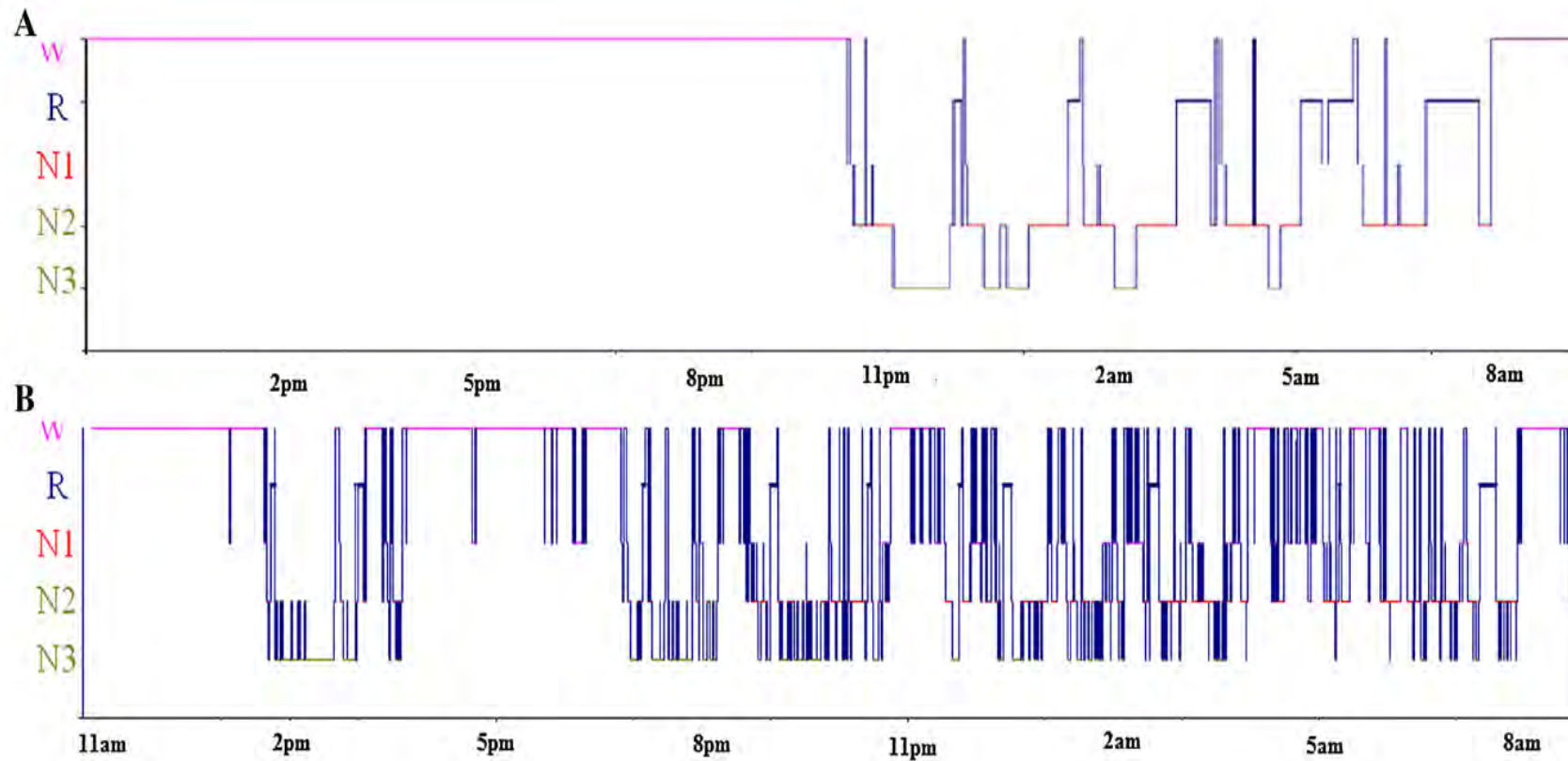
**Conclusions:** In conscious, mechanically ventilated patients, sleep architecture was highly abnormal, with a short REM stage and a high degree of fragmentation. The ventilatory mode did not influence sleep pattern, arousals, awakenings, and ineffective efforts.

*Cabello et al. Crit Care Med 2008*



Nuttapol Rittayamai  
Elizabeth Wilcox  
Xavier Drouot  
Sangeeta Mehta  
Alberto Goffi  
Laurent Brochard

## Positive and negative effects of mechanical ventilation on sleep in the ICU: a review with clinical recommendations



Normal hypnogram from a 62-year-old healthy subject.

N3 20% REM 26%

sleep hypnogram in a non-sedated 61-year-old patient during the weaning phase

N3 17% REM 7%

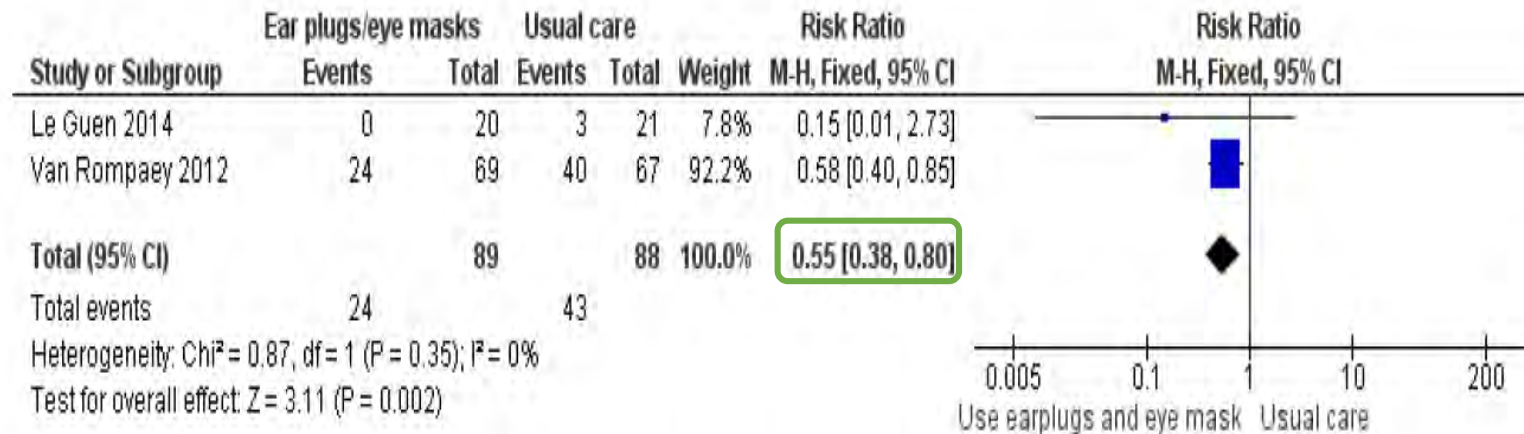
*Rittayamai N, et al. Intensive Care Med 2016*

# Traitement non-pharmacologique

# Non-pharmacological interventions for sleep promotion in the intensive care unit (Review)



Hu RF, Jiang XY, Chen J, Zeng Z, Chen XY, Li Y, Huining X, Evans DJW

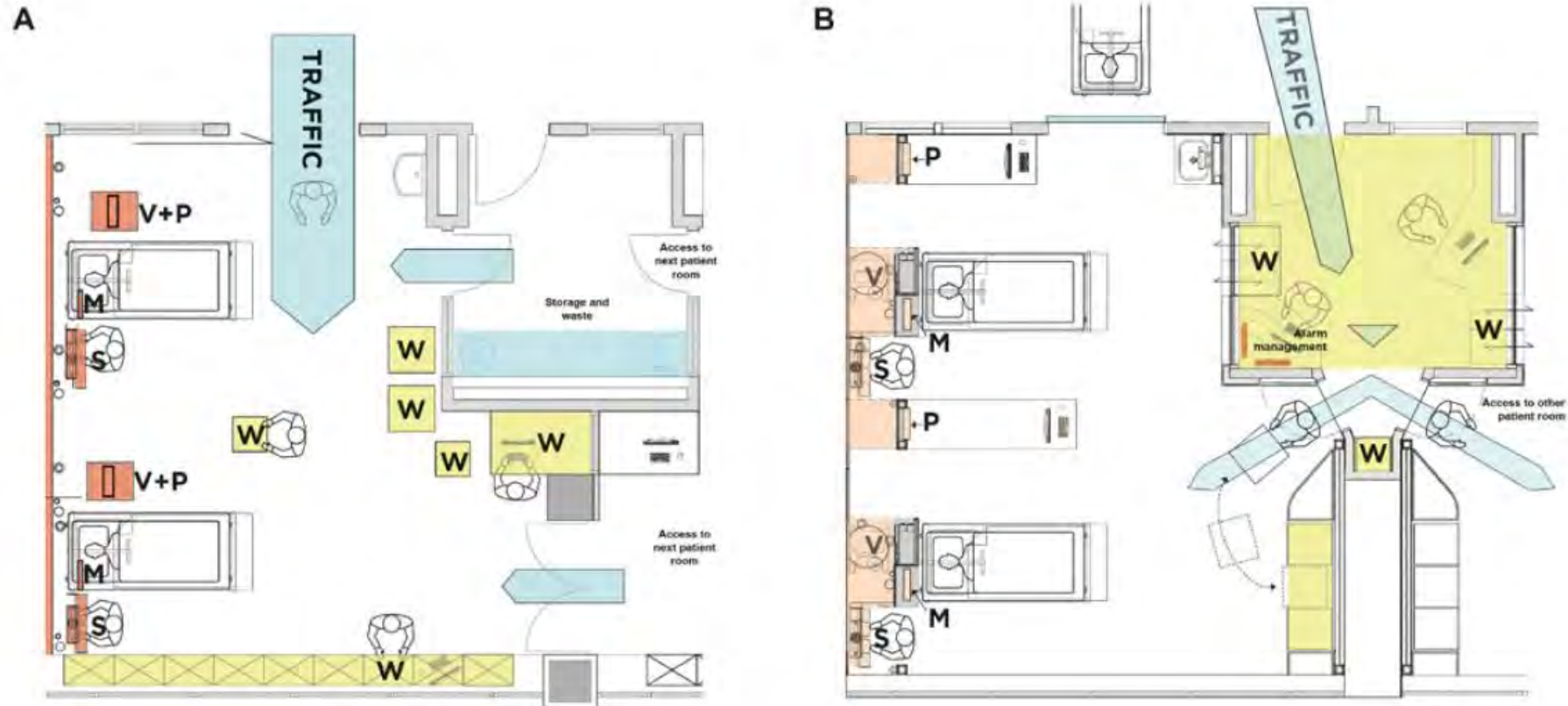


Our findings suggest that non-pharmacological interventions, such as the use of earplugs or eye masks or both, may have some beneficial effects on sleep promotion and potentially decrease the risk of delirium in intensive care unit (ICU) adult patients.

**Hu RF et al. Cochrane Database Syst Rev 2015**

# Feasibility of noise reduction by a modification in ICU environment

To cite this article: A Luetz *et al* 2016 *Physiol. Meas.* **37** 1041



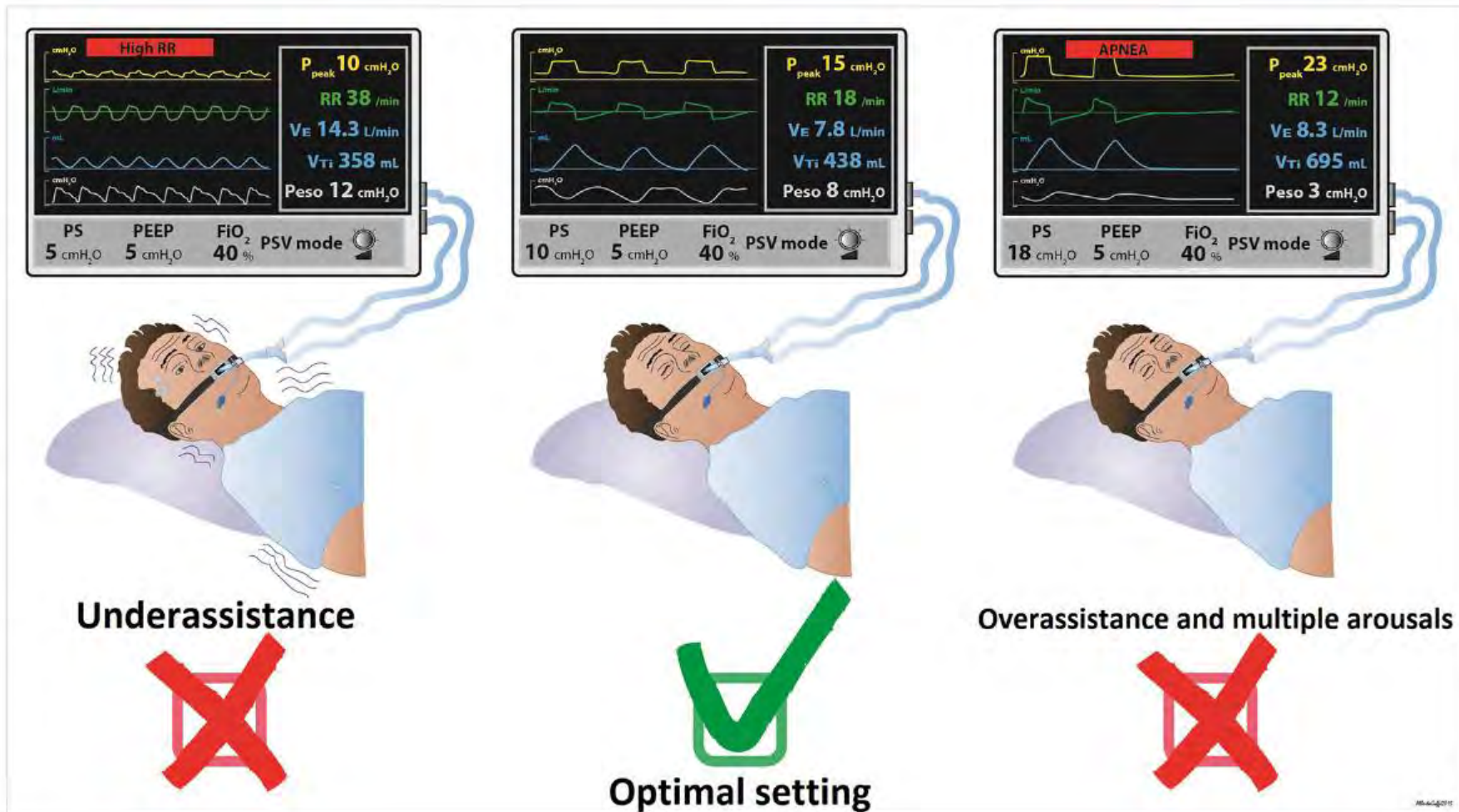
**Luetz A et al. *Physiol Meas* 2016**



**CHUV** Service de Médecine  
Intensive Adulte

*Luetz A et al. Physiol Meas 2016*

# Ventilation




*Rittayamai N, et al. Intensive Care Med 2016*

# Approche psychologique

Randomized clinical trial

## Randomized clinical trial of psychological support and sleep adjuvant measures for postoperative sleep disturbance in patients undergoing oesophagectomy

M. Scarpa<sup>1</sup> , E. Pinto<sup>1</sup>, E. Saraceni<sup>3</sup>, F. Cavallin<sup>1</sup>, M. Parotto<sup>5</sup>, R. Alfieri<sup>1</sup>, M. T. Nardi<sup>2</sup>, M. R. Marchi<sup>4</sup>, M. Cagol<sup>1</sup> and C. Castoro<sup>1</sup>, on behalf of the QOLEC Group\*

**Conclusion:** Perioperative psychological support reduces impairment in quality of life and quality of sleep after oesophagectomy. Registration number: NCT01738620 (<http://www.clinicaltrials.gov>).

***Scarpa M, et al. Br J Surg 2017***

# Traitement pharmacologique

# Time to Stop Counting Sheep in the ICU

**Dries Testelmans, MD, PhD**

**Bart Vrijsen, MSc**

**Bertien Buyse, MD, PhD**

Respiratory Division

University Hospitals Leuven

Leuven, Belgium



***Testelmans D, et al. Crit Care Med 2013***

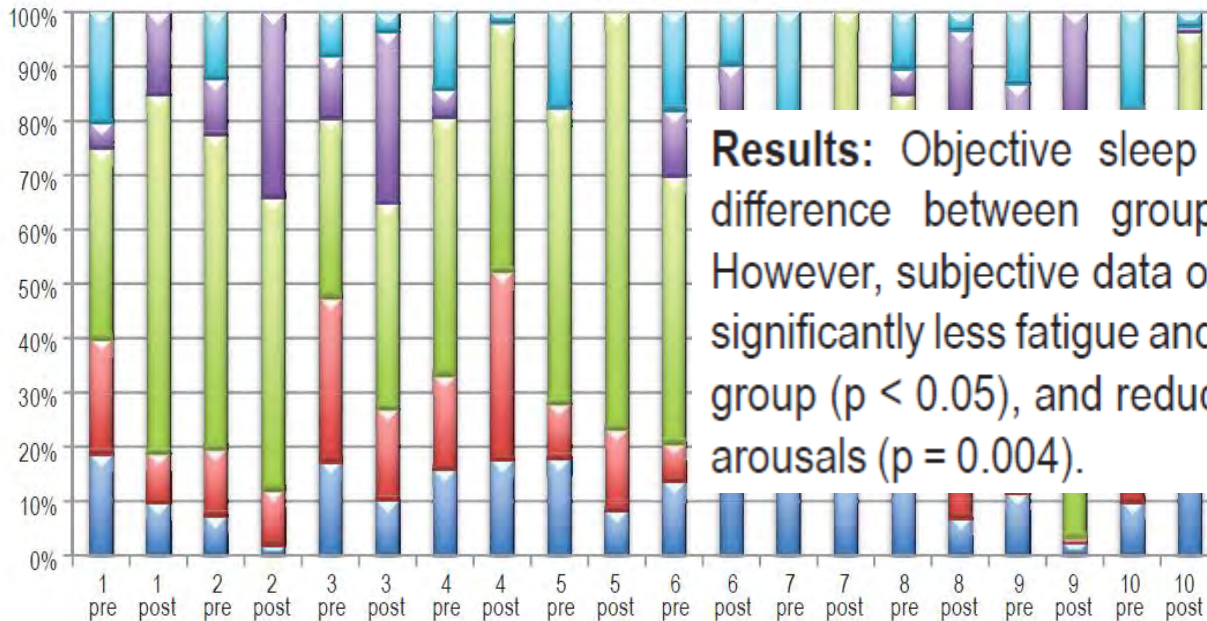
## Postoperative Sleep Disturbances after Zolpidem Treatment in Fast-Track Hip and Knee Replacement

Lene Krenk, M.D., Ph.D.<sup>1,2</sup>; Poul Jennum, M.D., Ph.D.<sup>3</sup>; Henrik Kehlet, M.D., Ph.D.<sup>1,2</sup>

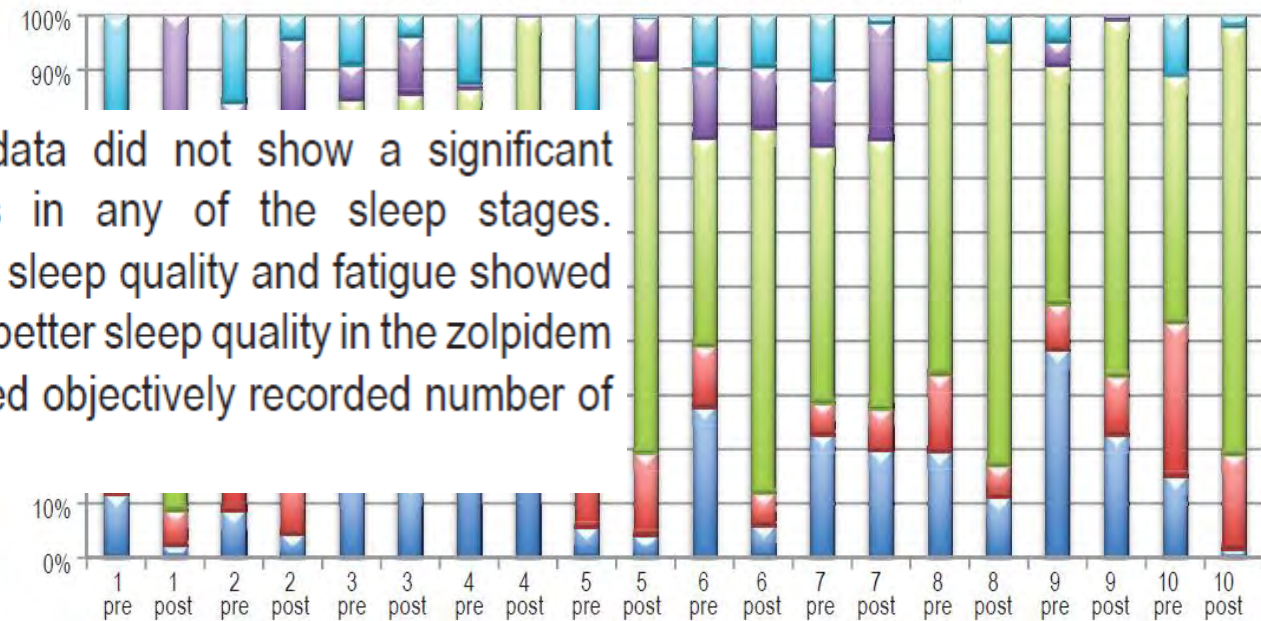
<sup>1</sup>Section of Surgical Pathophysiology, Rigshospitalet, University of Copenhagen, Denmark; <sup>2</sup>Lundbeck Centre for Fast-Track Hip and Knee Arthroplasty, Denmark; <sup>3</sup>Danish Centre for Sleep Medicine, Department of Clinical Neurophysiology, Glostrup Hospital, and Centre for Healthy Ageing, Faculty of Health, University of Copenhagen, Denmark



Sleep stage distribution in placebo group



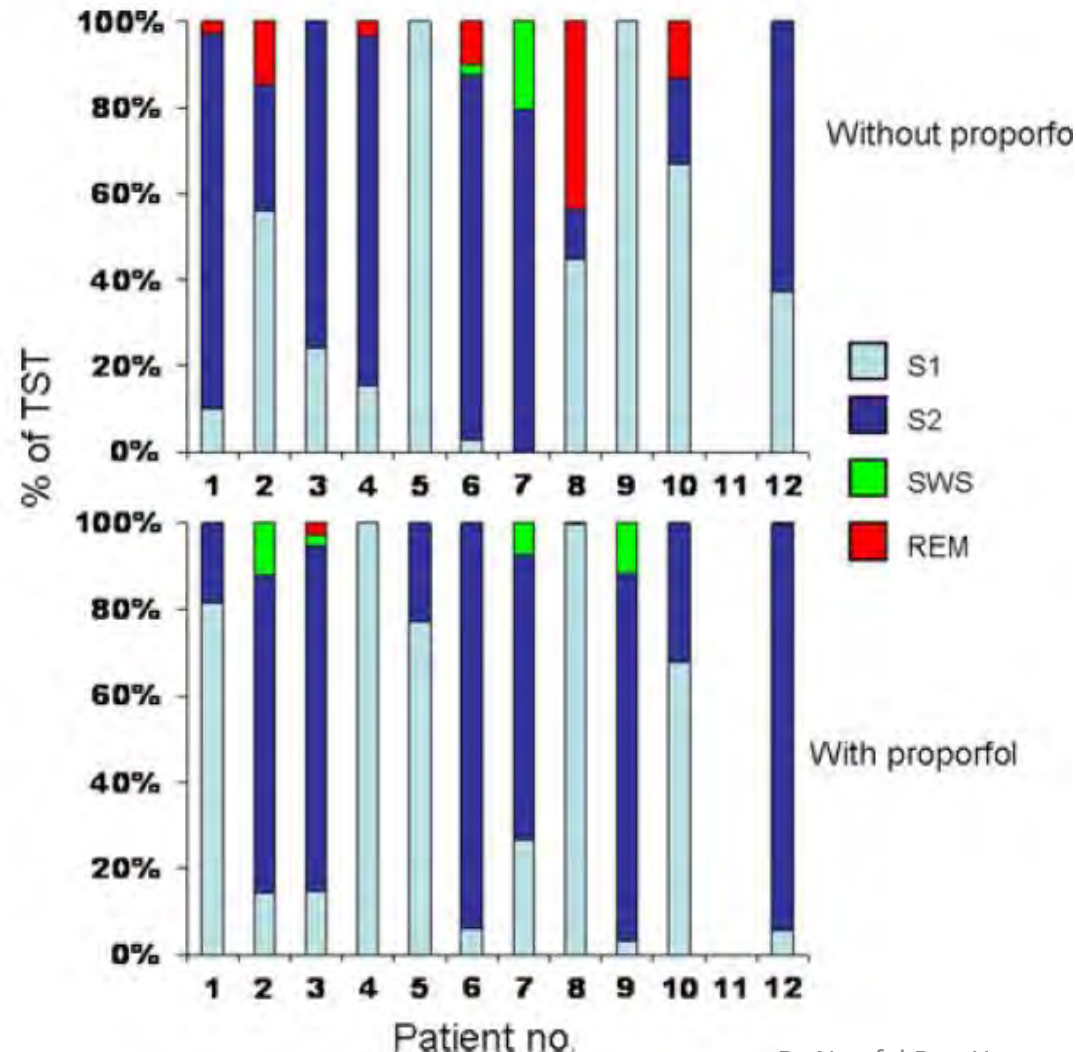
Sleep stage distribution in active treatment group



**Results:** Objective sleep data did not show a significant difference between groups in any of the sleep stages. However, subjective data on sleep quality and fatigue showed significantly less fatigue and better sleep quality in the zolpidem group ( $p < 0.05$ ), and reduced objectively recorded number of arousals ( $p = 0.004$ ).

n = 20 ( $\geq 60$  years) THA/TKA spinal anesthesia  
double-blind, randomized  
zolpidem 10 mg vs placebo

## Effects of propofol on sleep quality in mechanically ventilated critically ill patients: a physiological study



N = 12 MV patients  
PSG x 2 nights  
Propofol vs placebo  
Ramsay 3

*Conclusions:* In critically ill patients ventilated on assisted modes, propofol administration to achieve the recommended level of sedation suppresses the REM sleep stage and further worsens the poor sleep quality of these patients.

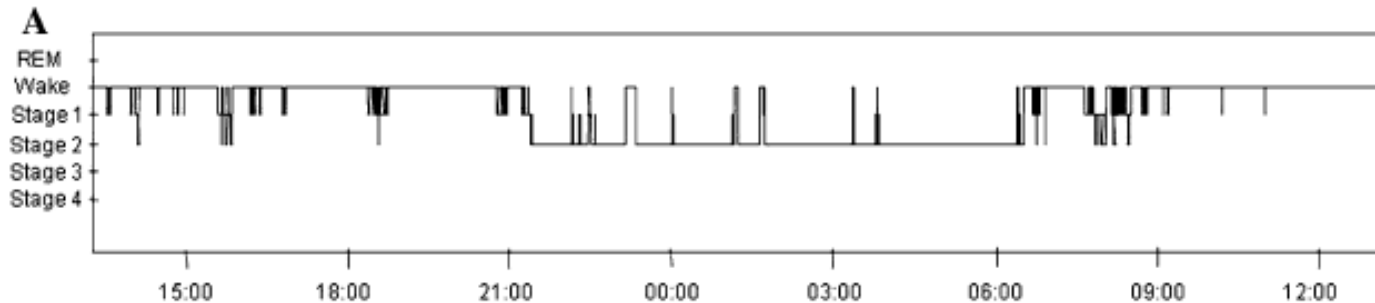
# Dexmedetomidine

Intensive Care Med (2012) 38:1982–1989  
DOI 10.1007/s00134-012-2685-y

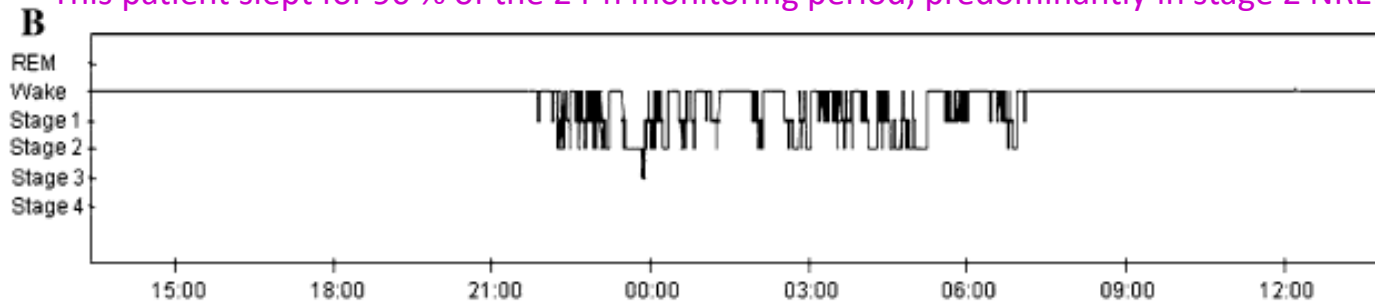
ORIGINAL

Jun Oto  
Katsunori Yamamoto  
Shigefumi Koike  
Mutsuo Onodera  
Hideaki Imanaka  
Masaji Nishimura

## Sleep quality of mechanically ventilated patients sedated with dexmedetomidine



This patient slept for 90 % of the 24-h monitoring period, predominantly in stage 2 NREM sleep



The patient had isolated episodes of stage 1 and 2 NREM sleep, but was awake for most of the 24-h monitoring period

PSG x 24h in MV patients

Dexmedetomidine 0.2-0.7  $\mu\text{g}/\text{kg}/\text{h}$  ad RASS -1/-4

*Conclusions:* In mechanically ventilated patients, nighttime infusion of dexmedetomidine preserved the day-night cycle of sleep but induced severely disturbed sleep architecture without evidence of SWS or REM sleep.

### Hypnograms of patients sedated with dexmedetomidine

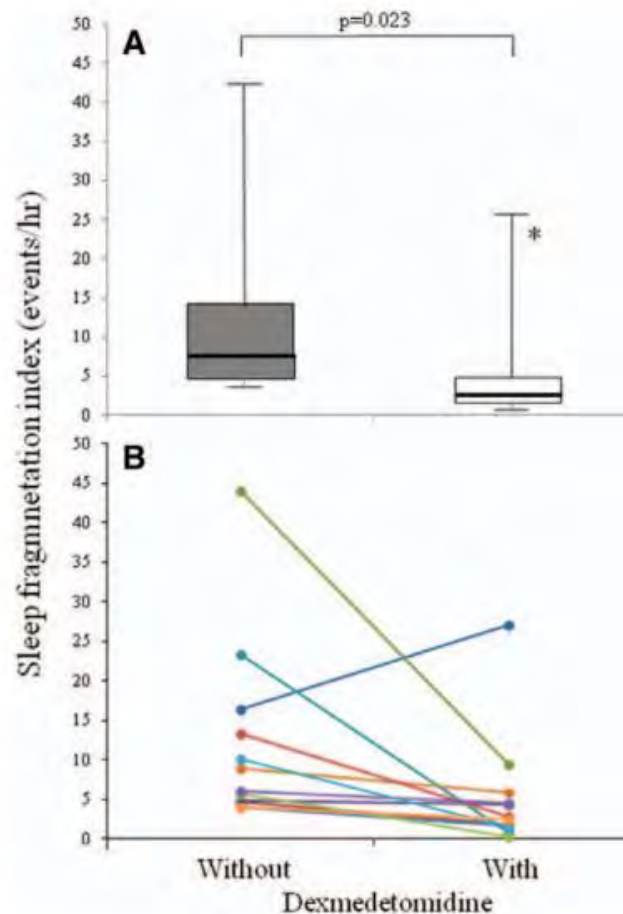
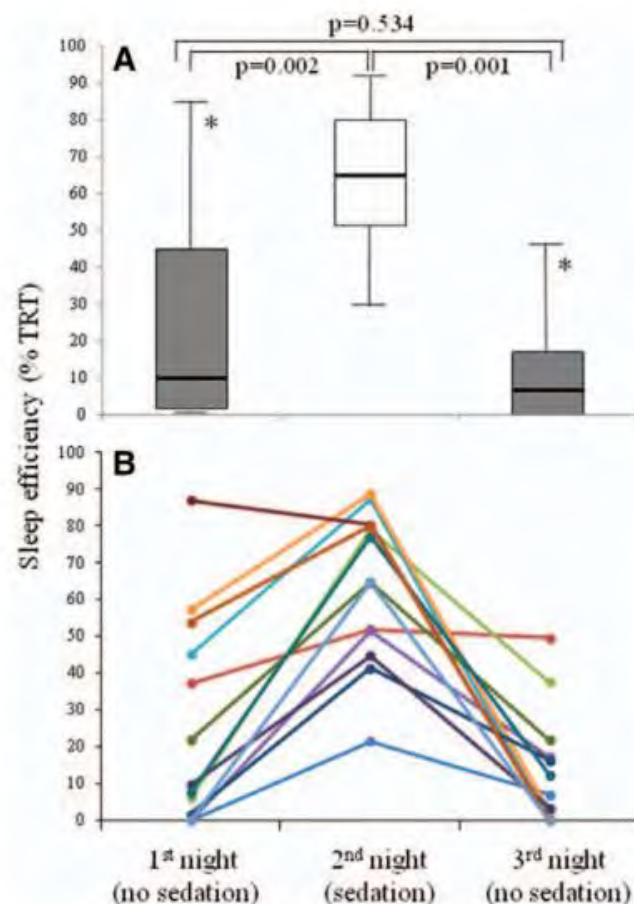
*Oto et al. Intensive Care Med 2012*

# Dexmedetomidine

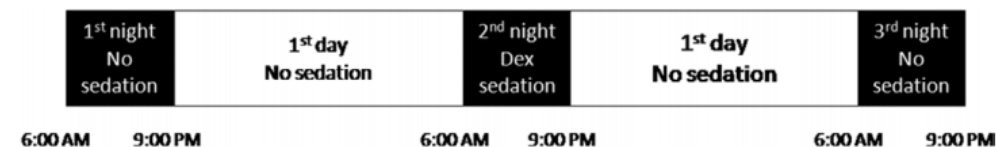
## Effects of Dexmedetomidine on Sleep Quality in Critically Ill Patients

### A Pilot Study

Christina Alexopoulou, M.D., Eumorfia Kondili, M.D., Eleni Diamantaki, M.D., Charalambos Psarologakis, M.D., Sofia Kokkini, M.D., Maria Bolaki, M.D., Dimitris Georgopoulos, M.D., Ph.D.



Dexmedetomidine 0.6 µg/kg/h RASS-1/-2  
N = 13 MV > 48h  
PSG x 57H

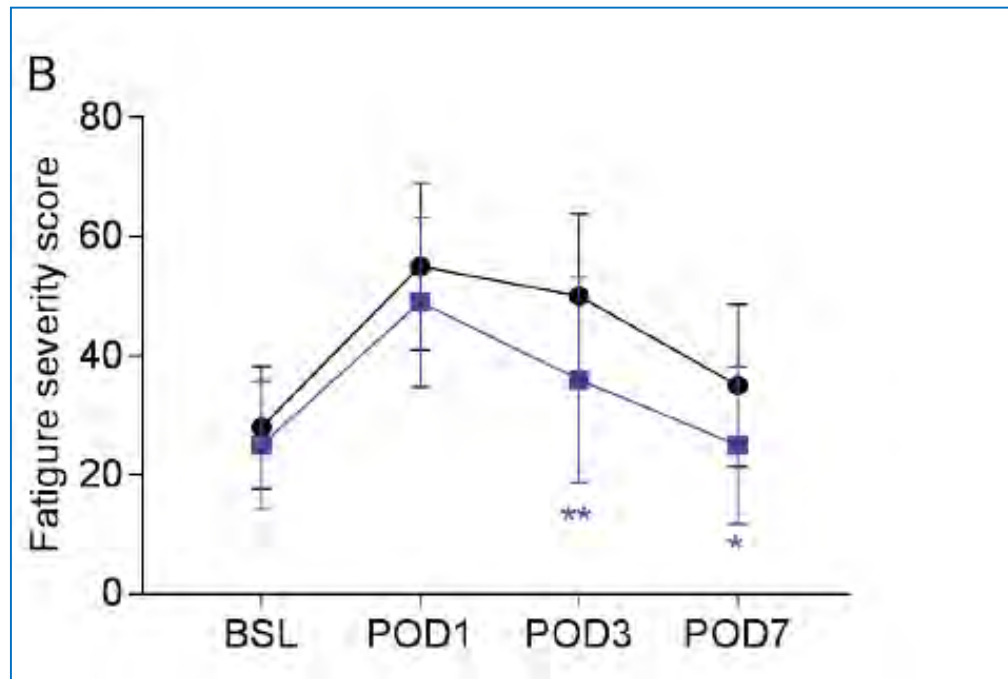


**Conclusion:** In highly selected critically ill patients, dexmedetomidine infusion during the night to achieve light sedation improves sleep by increasing sleep efficiency and stage 2 and modifies the 24-h sleep pattern by shifting sleep mainly to the night.

# Dexmedetomidine

**Intraoperative use of dexmedetomidine promotes postoperative sleep and recovery following radical mastectomy under general anesthesia**

Cunxian Shi<sup>1,\*</sup>, Jin Jin<sup>1,\*</sup>, Qiang Pan<sup>2</sup>, Shan Song<sup>1</sup>, Kezhong Li<sup>1</sup>, Jiahai Ma<sup>1</sup>, Tao Li<sup>1</sup> and Zhi Li<sup>1</sup>



N = 47

propofol/remifentanyl vs  
propofol/remifentanyl/Dexmedetomidine

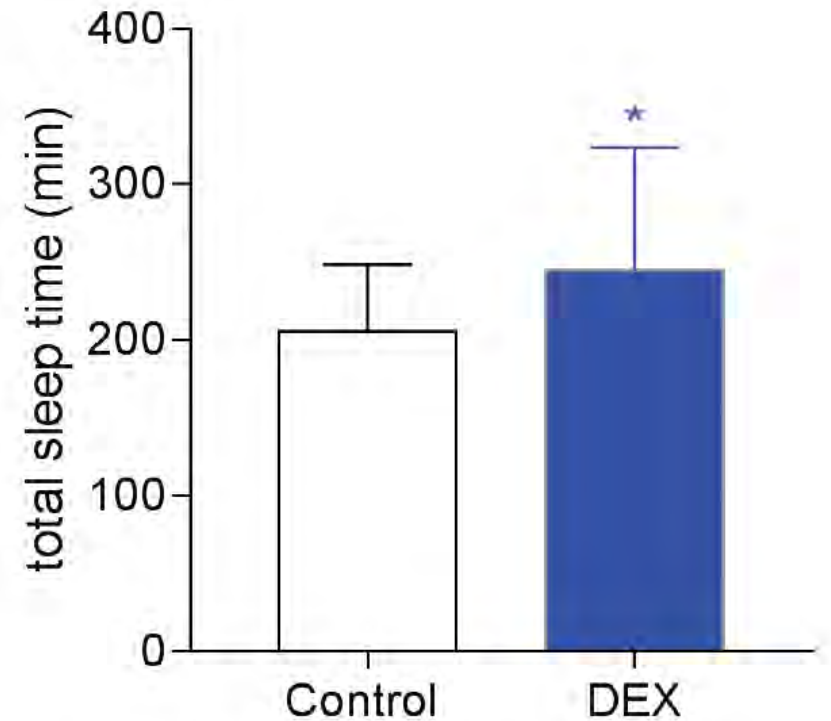


Figure 2: Postoperative 12 hour night sleep time from 8:00 PM to 8:00 AM. \* $P = 0.0381$ .

# Melatonin



August 2005 • www.clinicalneurologynews.com

Sleep Disorders

## FDA Approves Melatonin Agonist for Insomnia

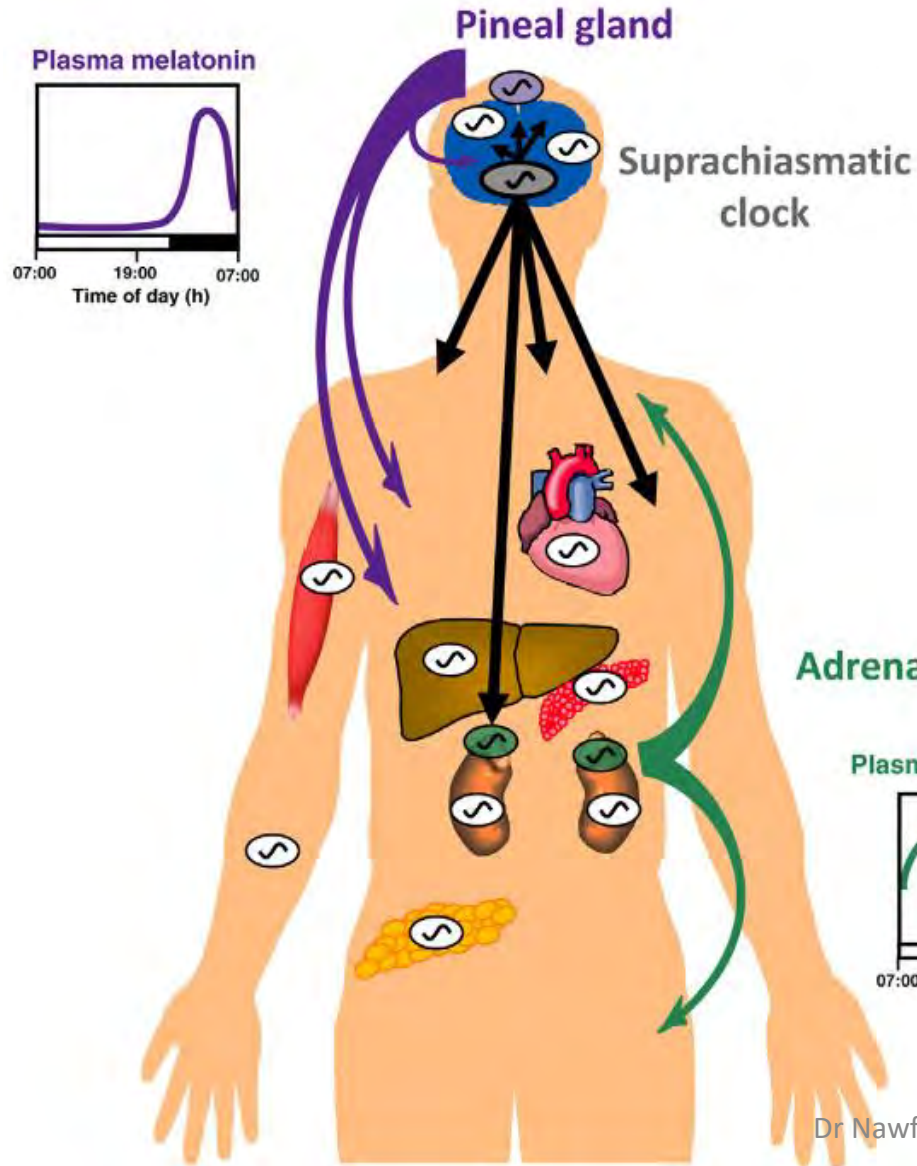
BY ELIZABETH MEHCATIE  
Senior Writer



Dr Nawfel Ben Hamouda - Sommeil aux SI 11.11.2022

<http://www.parapharmacie-naocia.com>

# Melatonin



Review Paper

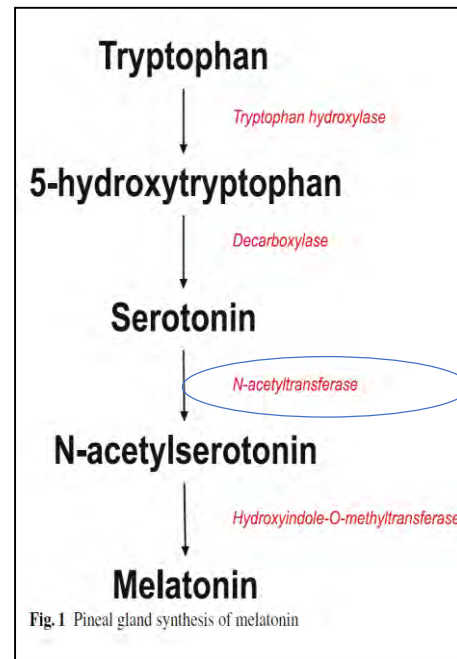
Melatonin: Both master clock output and internal time-giver in the circadian clocks network

Paul Pevet \*, Etienne Challet

Institut des Neurosciences Cellulaires et Intégratives, Département Neurobiologie des Rythmes, UPR 3212 CNRS, Université de Strasbourg, France

**Pevet P & Challet E. J Physiol Paris 2011**

# Melatonin



Drug group/drug	Proposed mechanism	Effect on melatonin serum concentration
Local anaesthetics	Inhibition of protein kinase C	—
Opioids	Opioid-mediated increase in NAT	+
Beta-blockers	CNS $\beta_1$ -receptor blockade	—
Benzodiazepines	GABA receptor agonism	—
Corticosteroids	Decreased NAT activity	—
Calcium channel blockers (dihydropyridine)	Decreased NAT activity	—
Nonsteroidal anti-inflammatory drugs	Inhibition of prostaglandin synthesis	—
Clonidine	$\alpha_2$ receptor agonism	—
Sodium valproate	Increased GABA levels	—

### Authors' conclusions

We found insufficient evidence to determine whether administration of melatonin would improve the quality and quantity of sleep in ICU patients. We identified sparse data, and noted differences in study methodology, in ICU sedation protocols, and in methods used to measure and report sleep.

Outcomes	Impacts	No of participants (studies)
<b>Quantity and quality of sleep as measured through reports of participants or of family members or by personnel assessments</b> Data collected at end of follow-up	In 1 study, participants completed the RCSQ and study authors reported no difference in SEI scores between groups. This was consistent with nurse assessment for which study authors also reported no difference in SEI scores between groups 2 studies reported no difference in duration of sleep observed by nurses	139 (3 studies)
<b>Quantity and quality of sleep as measured by PSG, actigraphy, BIS, or EEG</b> Data collected at end of follow-up	In 1 study, investigators used BIS and actigraphy to record sleep. Study authors reported no difference in SEI scores with both tools. Study authors also reported longer sleep in participants given melatonin which was not statistically significantly different, and also reported evidence of improved sleep in participants given melatonin from analysis of AUC using BIS data 1 study used PSG, with a large loss of participant data at follow-up	37 (2 studies)

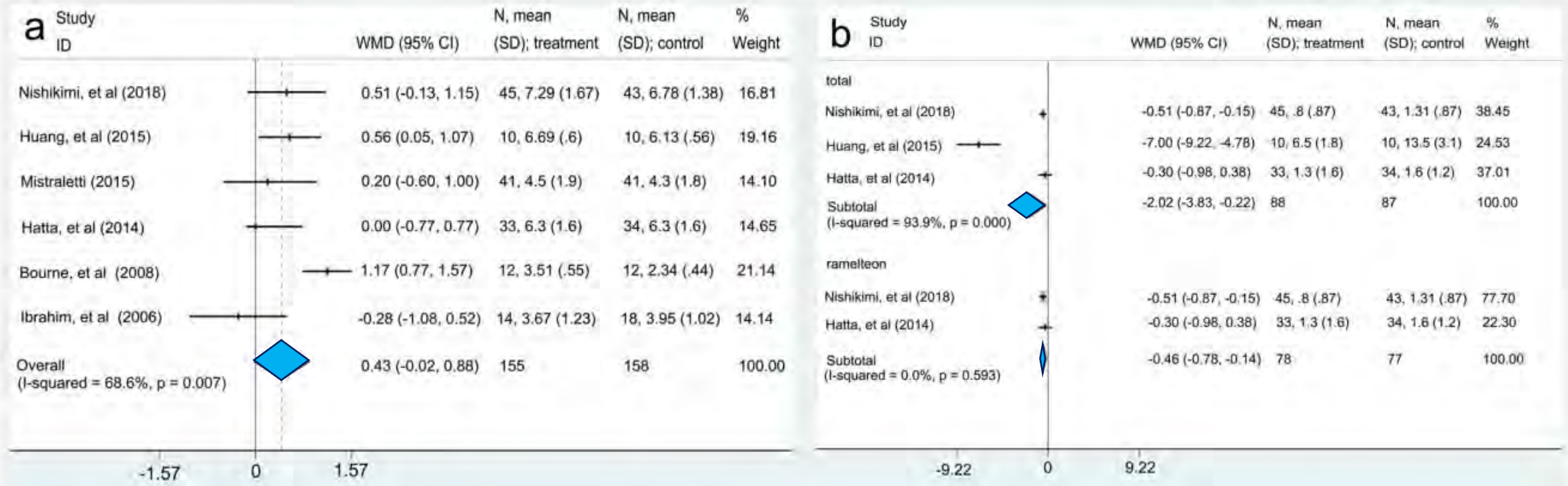
**3-10 mg melatonin**  
**At 8 or 9 pm**  
**3 - 7 nights**  
**Small n**

**Lewis SR, et al. Cochrane Database Syst Rev 2018**

# Melatonin

## Prophylactic use of exogenous melatonin and melatonin receptor agonists to improve sleep and delirium in the intensive care units: a systematic review and meta-analysis of randomized controlled trials

Qingyu Zhang<sup>1</sup> • Fuqiang Gao<sup>2</sup> • Shuai Zhang<sup>3</sup> • Wei Sun<sup>4</sup>  • Zirong Li<sup>2</sup>



Eight RCTs were included in the qualitative analysis. Administration of exogenous melatonin and melatonin receptor agonists was associated with a trend towards elongated duration of sleep (pooled weighted mean difference/WMD = 0.43; 95% confidence intervals/CIs, -0.02~0.88,  $p = 0.063$ ) and could decrease the number of awakenings per night (pooled WMD = -2.03; 95% CIs, -3.83~-0.22,  $p = 0.028$ ).

*British Journal of Anaesthesia* 112 (1): 7–8 (2014)  
doi:10.1093/bja/aet332

## EDITORIAL III

# Perioperative melatonin: not ready for prime time

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# Why?

# Melatonin

*Br. J. clin Pharmac.* (1985), **19**, 517–521

## Plasma concentrations of melatonin in man following oral absorption of different preparations

M. ALDHOUS, C. FRANEY, J. WRIGHT, & J. ARENDT

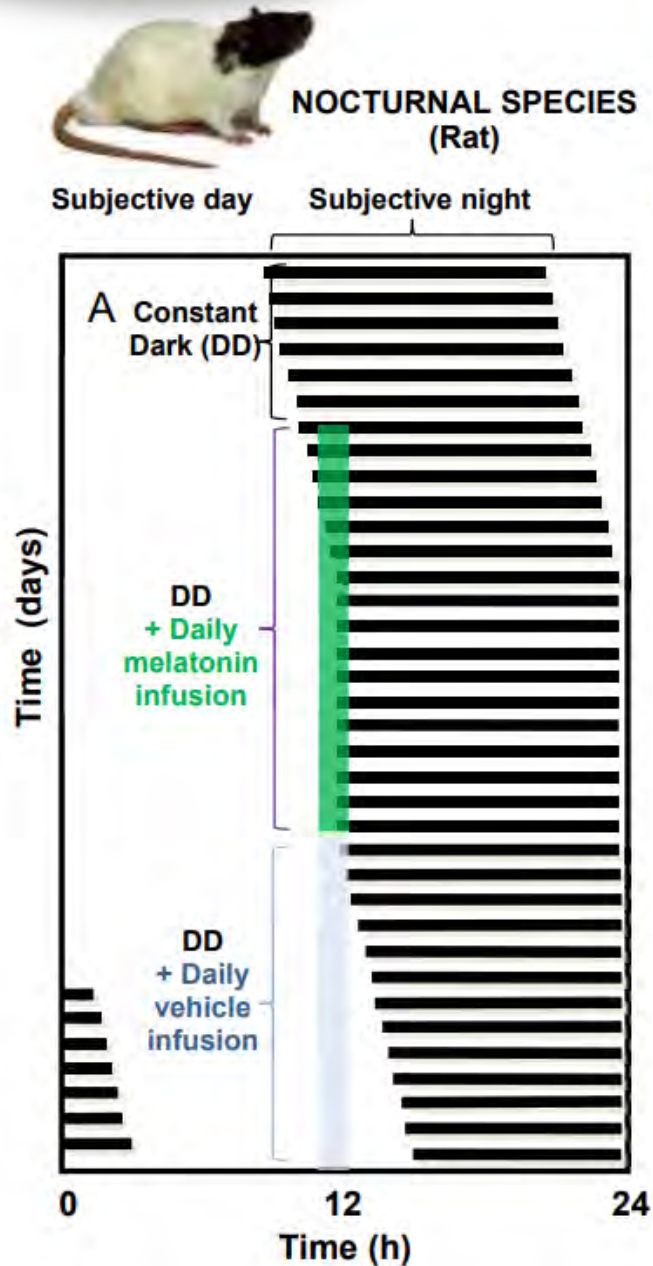
Department of Biochemistry, Division of Clinical Biochemistry, University of Surrey, Guildford, Surrey, UK

**Table 1** Areas under the plasma concentration curve (AUC, mean  $\pm$  s.e. mean), calculated to the limit of detectability above basal melatonin concentrations following ingestion of 2 mg melatonin as gelatine capsules or corn oil preparation.

<i>AUC</i> ( <i>pg ml<sup>-1</sup> h</i> )			
<i>Gelatine capsule</i>		<i>Corn-oil preparation</i>	
<i>Fed</i>	<i>Fasting</i>	<i>Fed</i>	<i>Fasting</i>
8036 $\pm$ 2455*	3712 $\pm$ 703	5826 $\pm$ 2644*	3953 $\pm$ 1533

\* $P < 0.05$ , fed compared to fasting, significance level assessed by paired Student's *t*-test.

Fed/fasting state ?



### The hormone melatonin: Animal studies

P. Pevet, Ph.D, Scientist \*, P. Klosen, Ph.D, Scientist,  
M.P. Felder-Schmittbuhl, Ph.D, Scientist

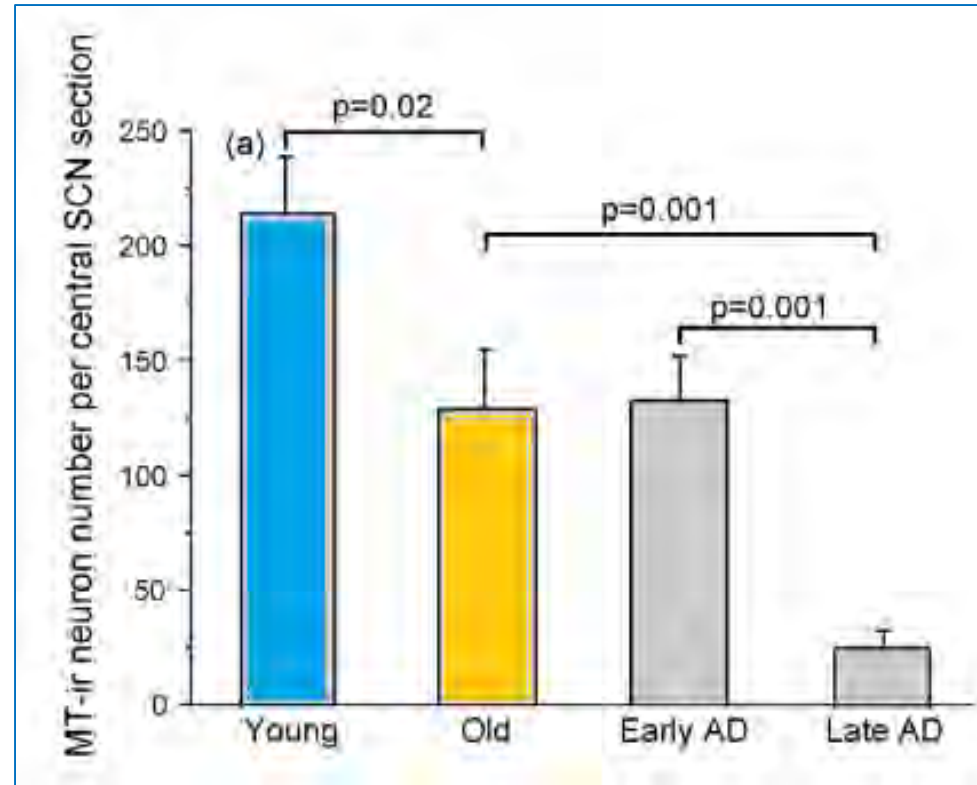
Institute for Cellular and Integrative Neurosciences (UPR 3212), CNRS and University of Strasbourg,  
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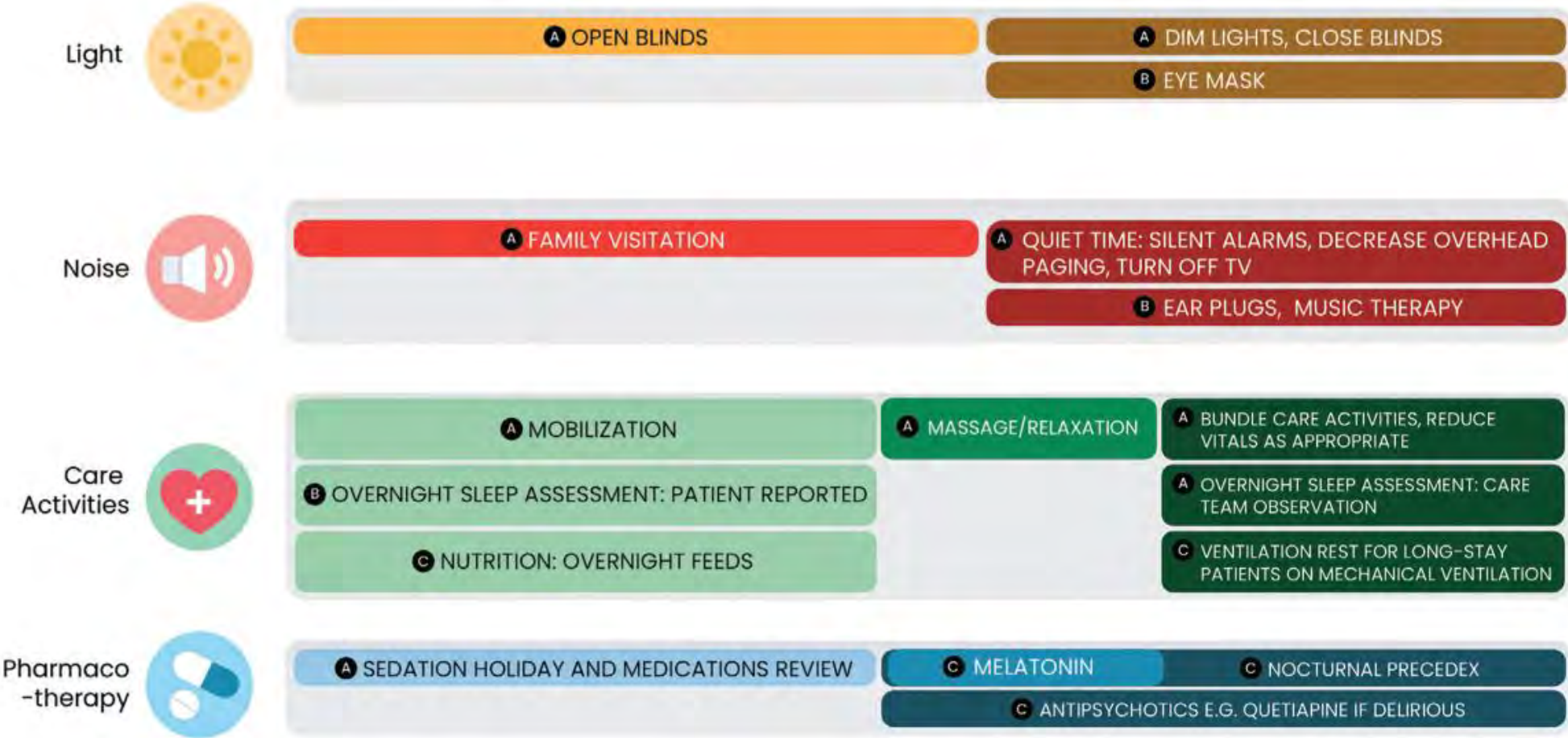


**Pevet et al. Best Pract Res Clin Endocrinol Metab  
2017**

Decreased MT1 melatonin receptor expression in the suprachiasmatic nucleus in aging and Alzheimer's disease

Ying-Hui Wu<sup>a</sup>, Jiang-Ning Zhou<sup>b</sup>, Joop Van Heerikhuize<sup>a</sup>,  
Ralf Jockers<sup>c,d,e,f</sup>, Dick F. Swaab<sup>a,\*</sup>





0700 0800 0900 1000 1100 1200 1300 1400 1500 1600 1700 1800 1900 2000 2100 2200 2300 0000 0100 0200 0300 0400 0500 0600 0700

**A** For all patients      **B** For non-delirious patients      **C** Additional therapies to be considered and individualized

*Lee EY & Wilcox ME.  
Curr Op Pulm Med 2022*

# Conclusion

**Importance du sujet**

**Conséquences court et moyen terme**

**Prévention**