Sleep disturbance and circadian disruption in critically ill patients

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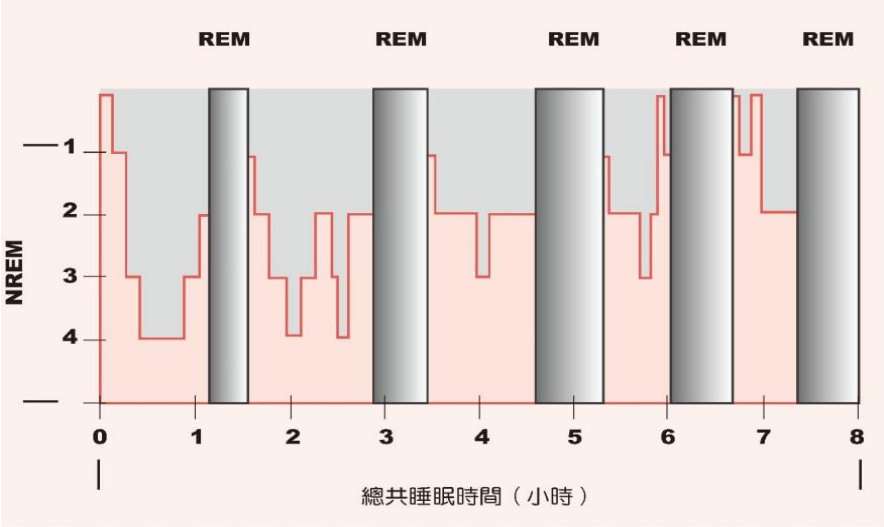
Highlight

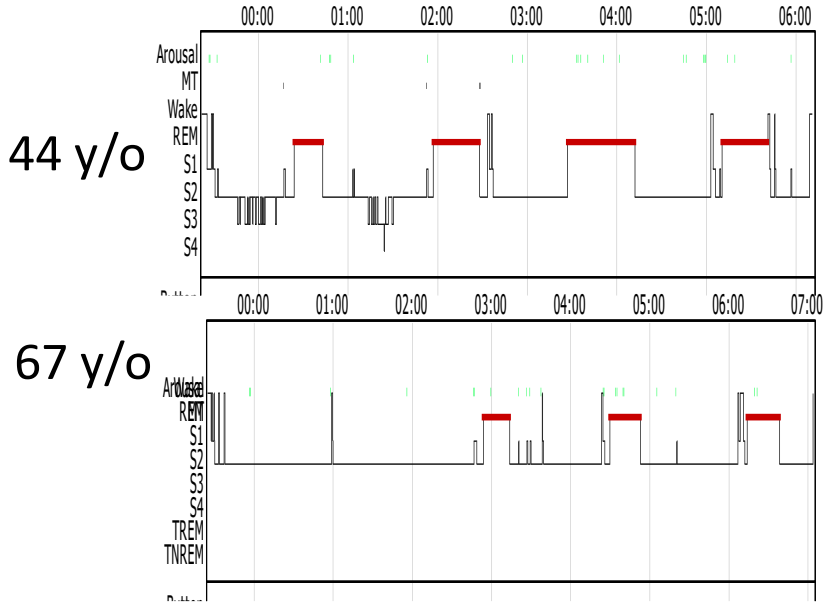
- Physiology of sleep and circadian
- Sleep homeostasis
- Measurement of chronotype and sleep
- Luminance, circadian and sleep
- PADIS: actionable patient intervention

Physiology of sleep

- 一個睡眠週期約90分鐘，一個晚上有4~5個週期，睡眠週期分為非快速動眼期 (NREM)跟快速動眼期 (REM)
- 深睡期(S為身體休息與內分泌激素分泌，如生長激素
- 夢境與日間學 整合成記憶 則發生在快速動眼期

Sleep stage hypnogram





Borbély Hum Neurobiol. 1982;1(3):195

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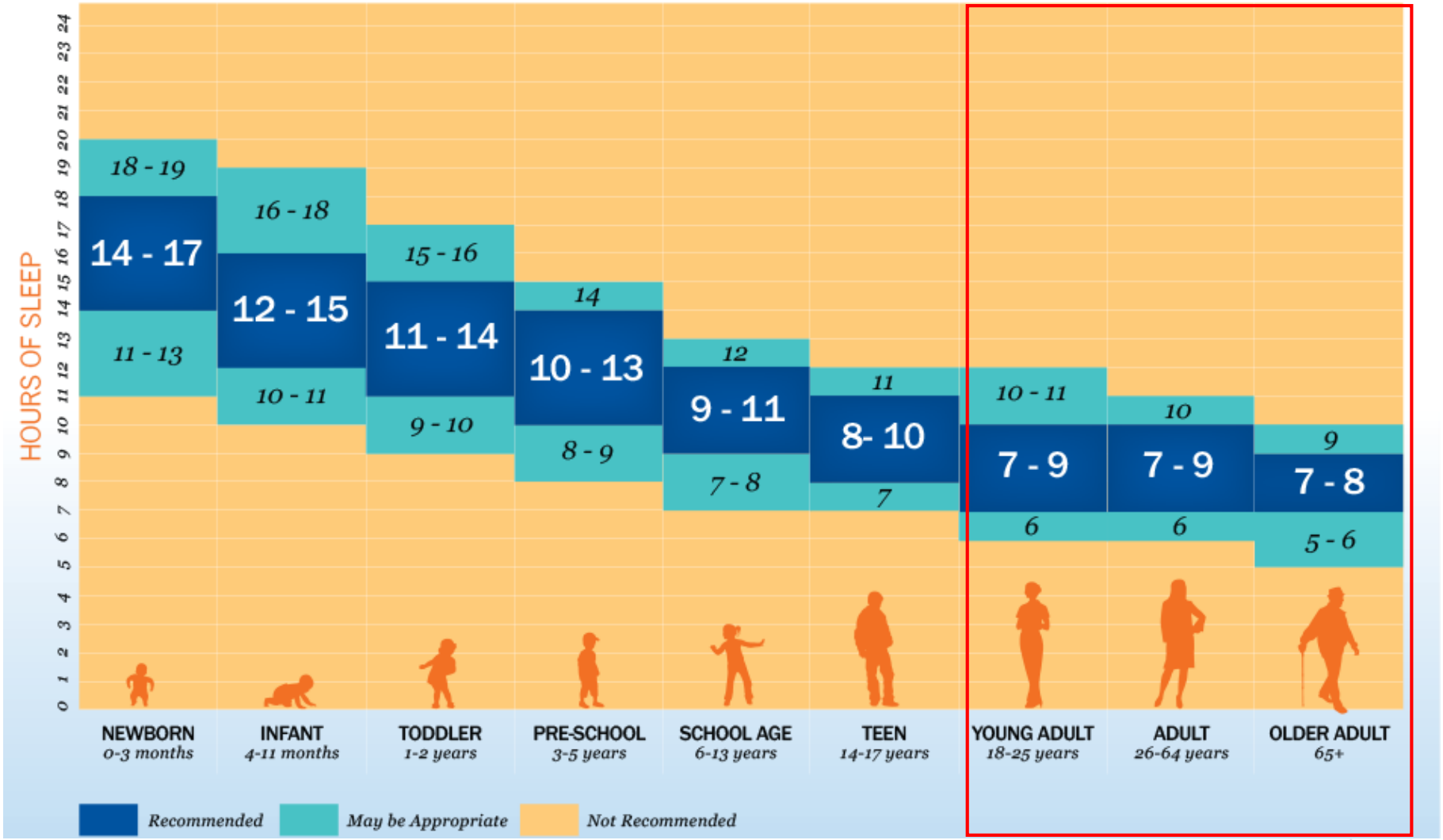
Sleep duration recommondation



Hirshkowitz M. Journal of the National Sleep Foundation 2015

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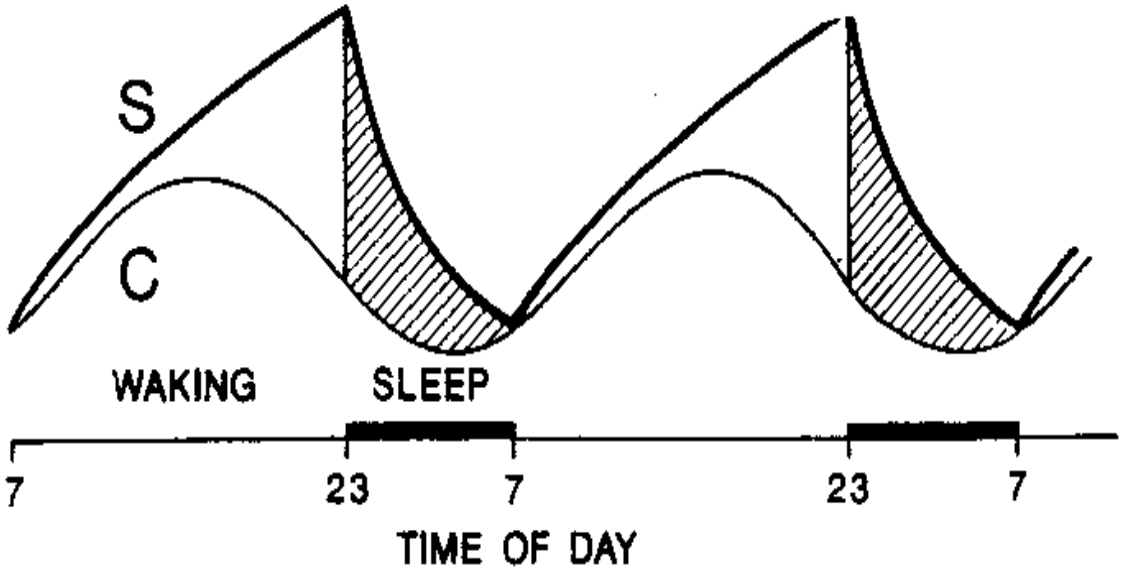
Sleep homeostasis: sleep driving vs circadian



- Circadian biomarker
  - Melatonin
  - Cortisol
  - TSH
  - Core temperature
  - Urine output
- Intrinsic clock: free running, 24-25 hr
- Solar clock vs social clock
- Entrainment vs detrainment

Borbély Hum Neurobiol 1982

Chronobiologic monitoring techniques

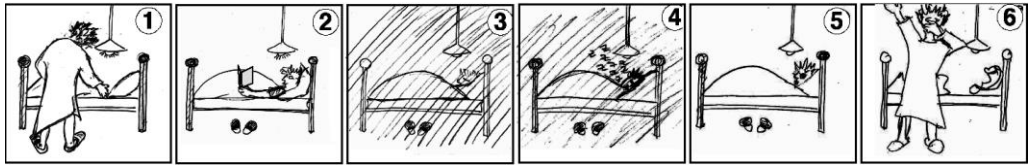
- Subjective
  - Munich ChronoType Questionnaire (MCTQ)
- Objective
  - 3 -14 day actiwatch
  - Salivary or plasma melatonin or cortisol
    - DLMO: evening rise in blood levels of melatonin (approximately 10.75 hours before wakeup time)
    - DLM offset: decline in blood levels of melatonin
    - Sensitivity 1ng/L

Smith MT. J Clin Sleep Med. 2018

Assessment of chronotype: MCTQ

- Munich ChronoType Questionnaire (MCTQ)
  - Shift vs no shift

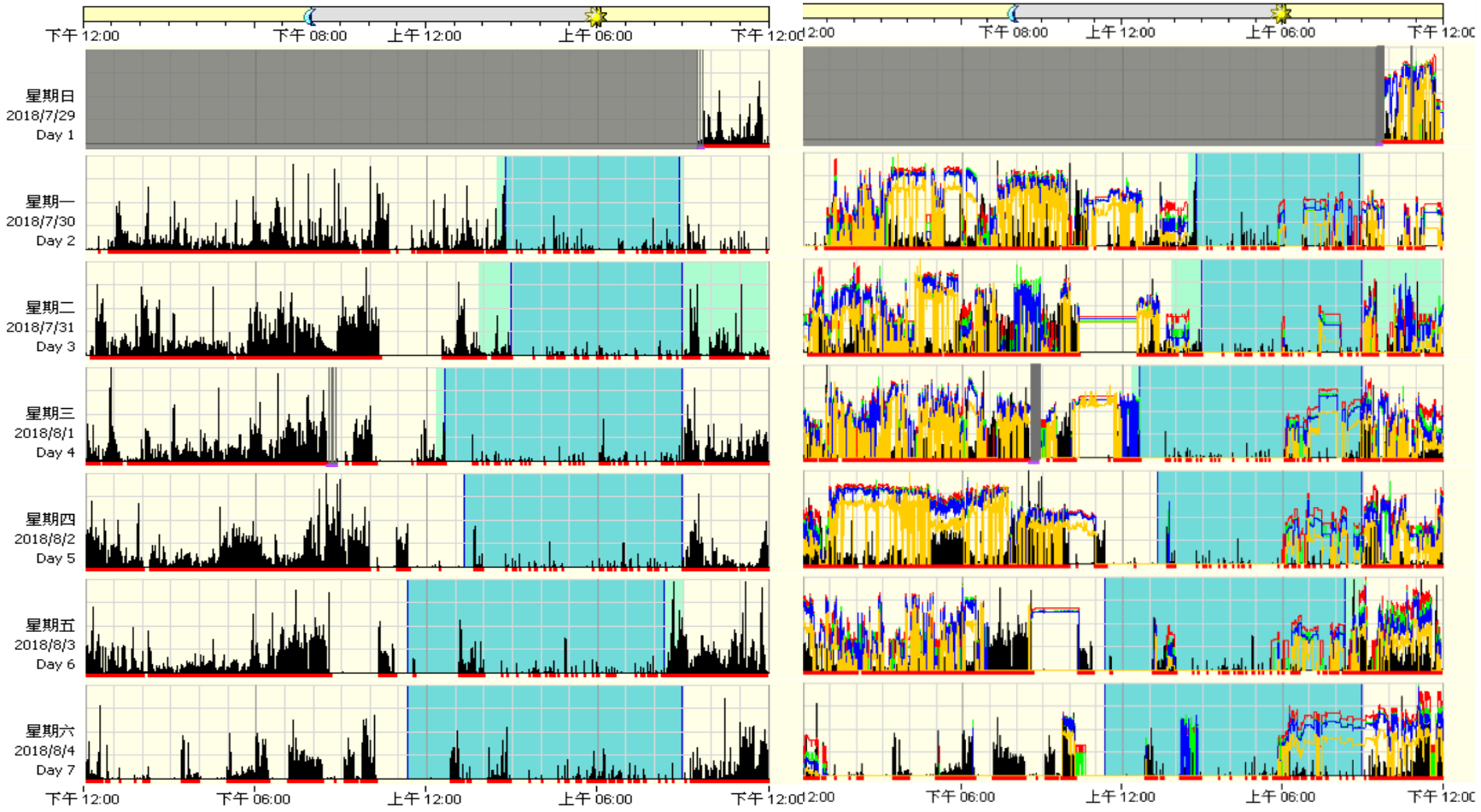
How to fill out the Munich ChronoType Questionnaire:



- Midsleep
  - Bedtime + sleep onset + sleep duration/2
    - Weekday: W1-4, W7 night (MSF); free day: W5-6 night (MSW)
- Social jet lag=MSF- MSW

Roenneberg T. Journal of Biological Rhythm 2003; Juda M. Journal of Biological Rhythm 2013; Cheng WJ. Chronobiology International 2017.

Actigraph: objective measurement habitual sleep-wake



	Avg
Time in Bed (hr)	8:19:17
Total Sleep Time (hr)	6:44:38
Onset Latency (min)	14.43
Sleep Efficiency (%)	81.85
WASO (min)	40.07
#Awak.	41.29

Activity Scale: 853/0, White Light Scale: 145396.0/0.1, Color Light Scale: 2.997E+03/1.000E-02

Smith MT. J Clin Sleep Med. 2018

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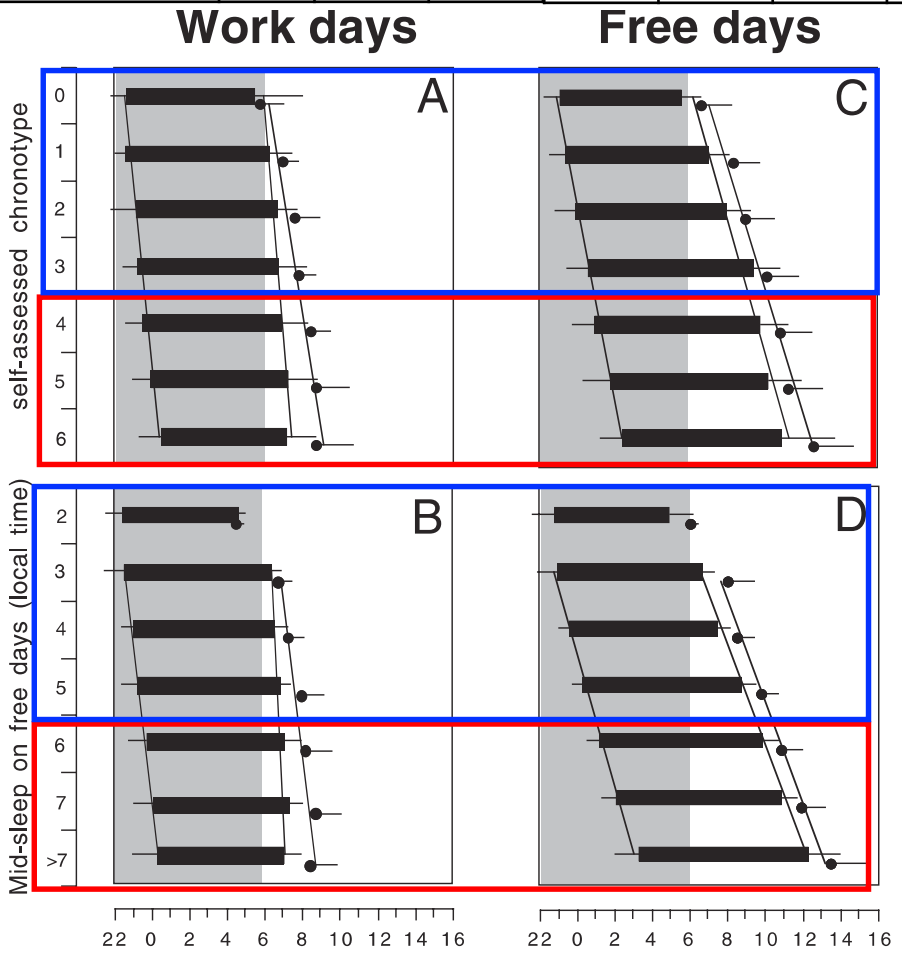
Sleep patterns of different chronotypes

chronotype	1	2	3	4	5	6	7
	EE	ME	SE	N	SL	ML	EL



- Early chronotypes suffer from staying late to comply with social activity
  - Early chronotypes wake up too early on free days
- Late chronotypes suffer from too early on workdays

Roenneberg T. Journal of Biological Rhythm 2003

Measurement of sleep

- Subjective
  - Habitual sleep pattern: sleep log
  - Sleep quality:
    - Non-critically ill: Pittsburgh Sleep Quality Index (PSQI); visual analog scale
    - Critically ill: Leeds Sleep Evaluation Questionnaire (LESQ); Richards-Campbell sleep questionnaire (RCSQ)
- Objective
  - Polysomnography
  - Actiwatch
  - Single lead EEG

Sleep log: subjective measurement of habitual sleep-wake

早上填寫(隔天)

範	例							
日　期	11/20	7/25	7/26	7/27	7/28	7/29	7/30	7/31
星期幾	星期一	星期六	星期日	星期一	星期二	星期三	星期四	星期五
是否使用任何幫助睡眠的物質?是什麼	有。熱牛奶	無	無	無、	無	無	無	;
就寢時間(躺上床的時間)(*請見下方說明)	11:30PM	AM 02:30	AM 02:20	AM 04:40	AM 06:30	AM 01:00	AM 08:00	AM 04:00
睡著所需時間	45 分鐘	30分鐘	30分鐘	40分鐘	20分鐘	20分鐘	30分鐘	15分鐘
醒來的次數	4	7	1	3	2	1	3	2
總計睡眠時間	6 小時	8小時	8小時	8小時	8小時	8小時	5小時	7小時
起床時間(*請見下方說明)	7:00AM	AM 11:30	AM 11:40	PM 02:00	PM 03:00	PM 09:30	PM 02:00	AM 11:00
起床時感覺如何?(**請見下方說明)	3	3	3	2~3	2~3	2	1	2

下午填寫(當天)

範	例							
日　期	11/20	7/25	7/26	7/27	7/28	7/29	7/30	7/31
星期幾	星期一	星期六	星期日	星期一	星期二	星期三	星期四	星期五
你是否有小睡?(時間、多久)	1:00PM/10 分鐘 5:00PM/50 分鐘	無	無	無	無	無	無	無
有喝酒嗎?(時間、多久)	5:00PM/2	無	無	無、	6:30 PM 7/29 02:30 AM 有	無	6:30 PM 7/31 02:00 AM 有	無
有使用咖啡因飲料嗎?(咖啡、茶...等)(時間、次數)	8:00AM/4 2:00PM/2	無	無	無	無	無	無	無
你中午時感覺如何(**請見下方說明)	2	2	3	3	2	2	1	2
你下午時感覺如何(**請見下方說明)	2	2	2	3	2	2	1	2

- Parameter
  - Time in bed (TIB)= time to wake up-time to bed
  - Time to try to fall asleep
  - Minute to fall asleep (SOL)
  - Hour of sleep
  - Wake after sleep onset (WASO)
  - Sleep quality
  - Sleep efficiency=hour of sleep/TIB

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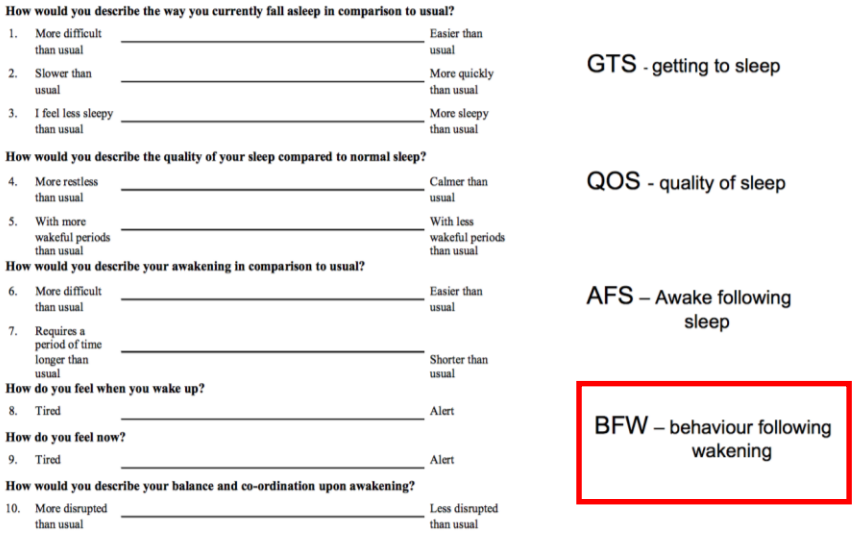
Evaluation of sleep disturbance in critically ill patients

- Leeds Sleep Evaluation Questionnaire (LESQ)
  - Subjectively perceived changes in sleep and next morning behavior



How would you describe the way you currently fall asleep in comparison to usual?

1.	More difficult than usual	Easier than usual
2.	Slower than usual	More quickly than usual
3.	I feel less sleepy than usual	More sleepy than usual

How would you describe the quality of your sleep compared to normal sleep?

4.	More restless than usual	Calmer than usual
5.	With more wakeful periods than usual	With less wakeful periods than usual

How would you describe your awakening in comparison to usual?

6.	More difficult than usual	Easier than usual
7.	Requires a period of time longer than usual	Shorter than usual

How do you feel when you wake up?

8.	Tired	Alert

How do you feel now?

9.	Tired	Alert

How would you describe your balance and co-ordination upon awakening?

10.	More disrupted than usual	Less disrupted than usual

GTS - getting to sleep

QOS - quality of sleep

AFS – Awake following sleep

BFW – behaviour following wakening

- Richards-Campbell sleep questionnaire (RCSQ)
  - Perceptions of depth of sleep
  - Sleep onset latency
  - Number of awakenings
  - Time spent awake
  - Overall sleep quality

Parrott AC. 1978 Psychol Med. 1978; Richards KC J Nurs Meas. 2000; Chen LX Nurs Crit Care. 2019

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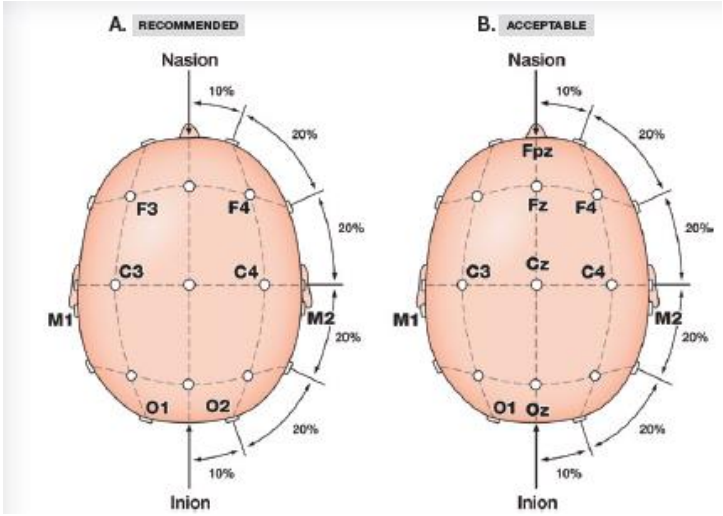
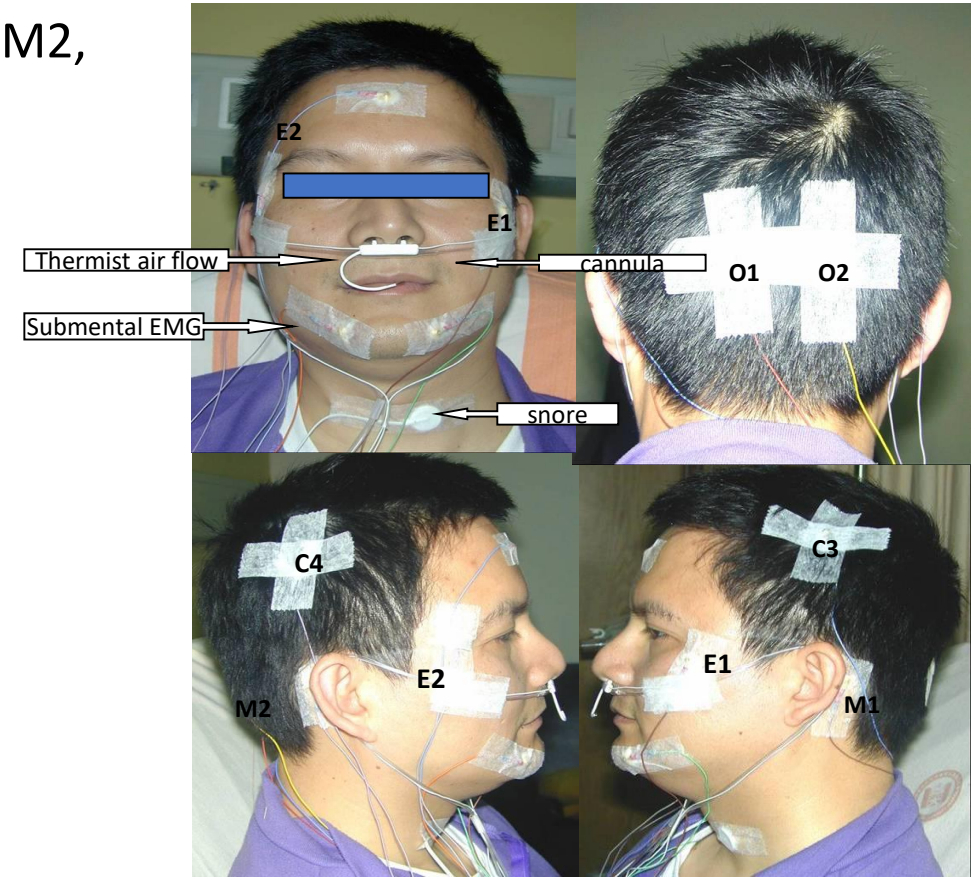
Polysomnography: montage

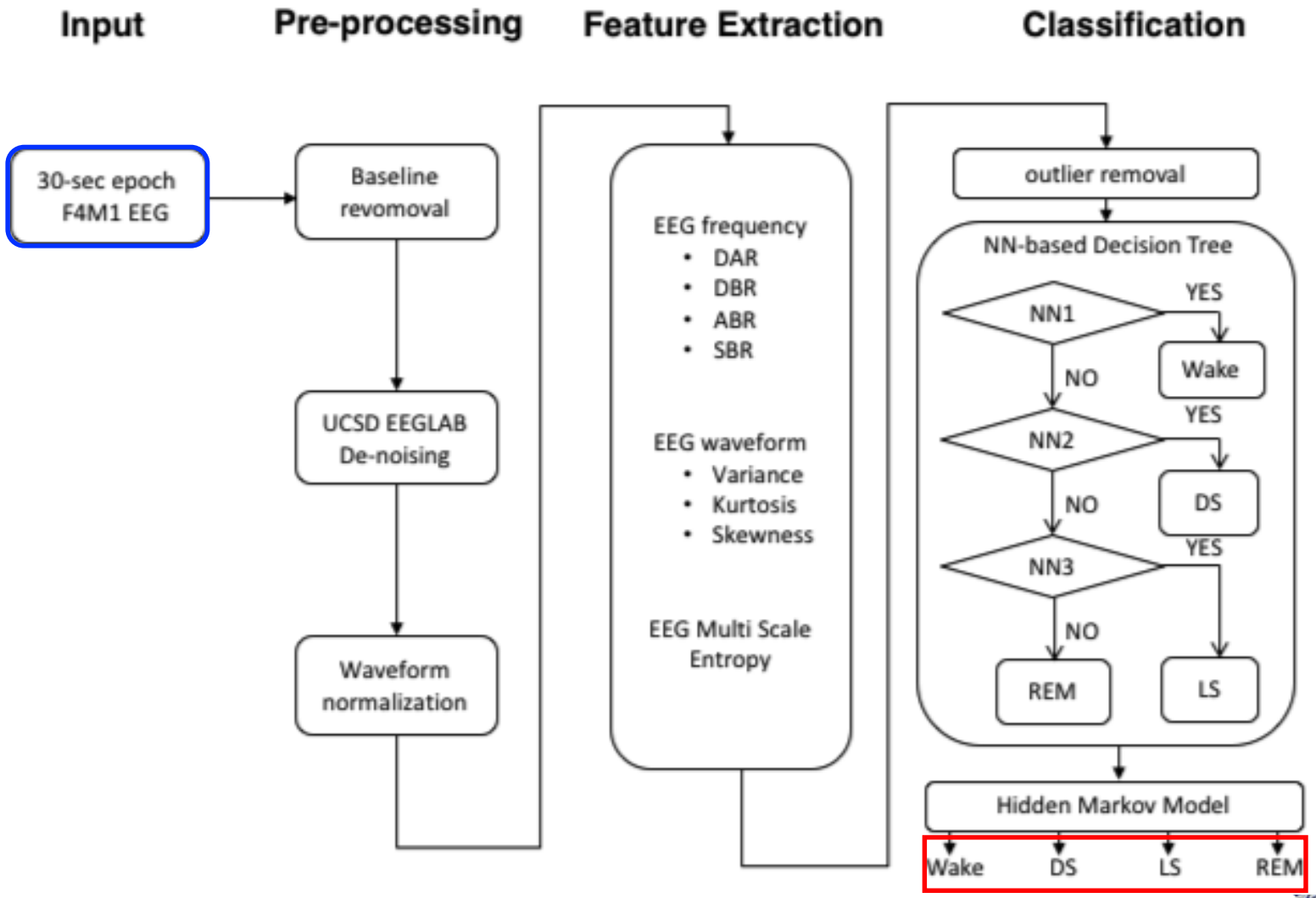
- EEG:F4-M1, C4-M1, O2-M1, F3-M2, C3-M2, O1-M2
- EOG: E1-M2, E2-M2
- Submental EMG: 3 electrode





Berry RB. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Speci cations. Version 2.4

Automatic sleep staging in patients with OSA using single-channel frontal EEG

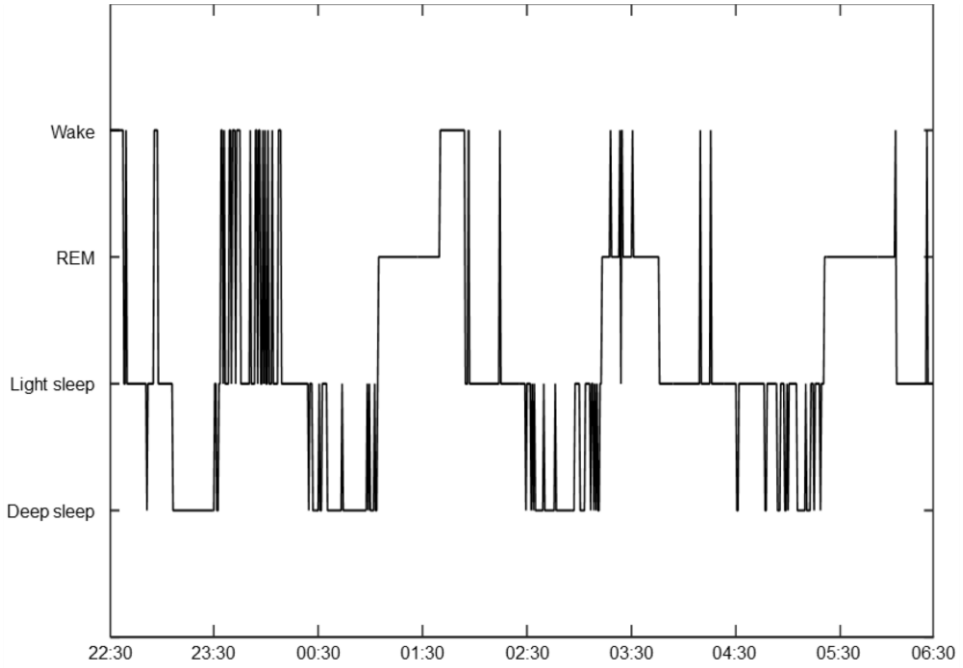


DS: deep sleep
LS: light sleep

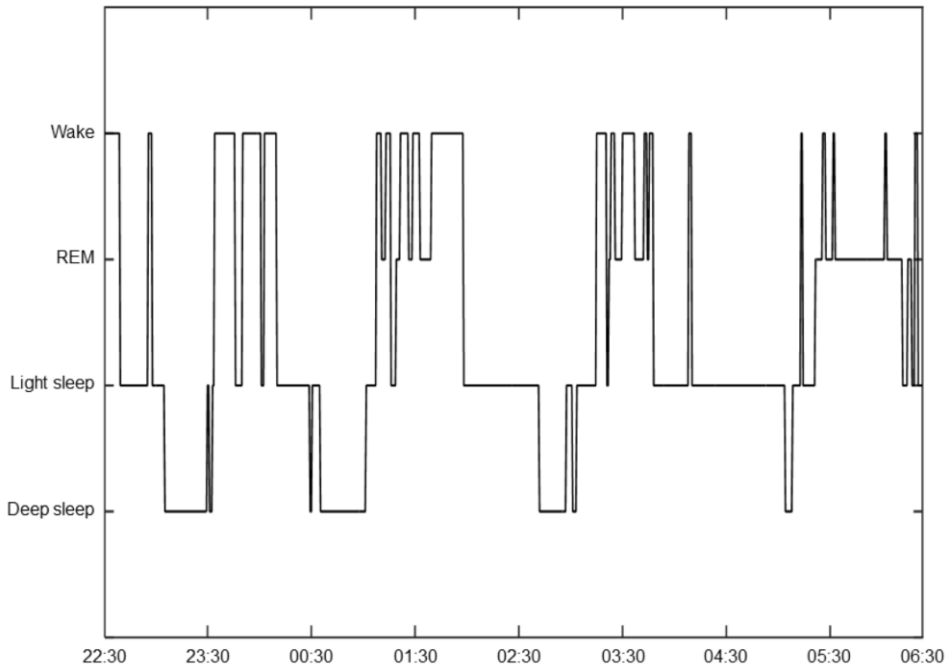
Lee PL. J Clinical Sleep Med 2019

Representative whole-night sleep stages

Expert scoring



Automatic sleep staging system



Lee PL. J Clinical Sleep Med 2019

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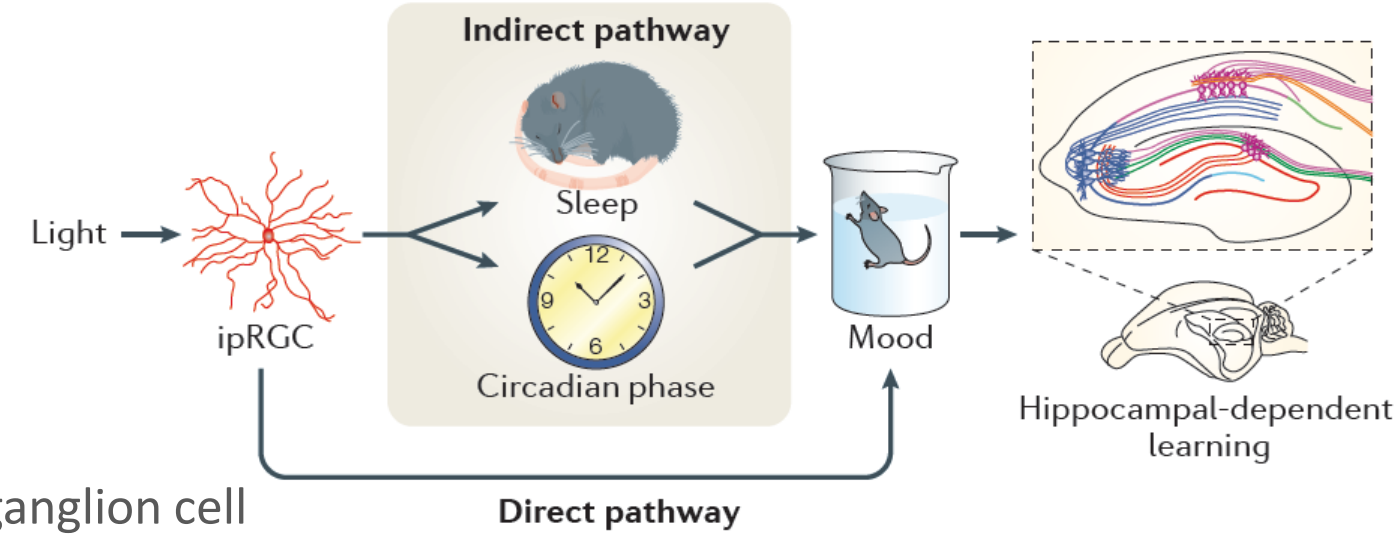
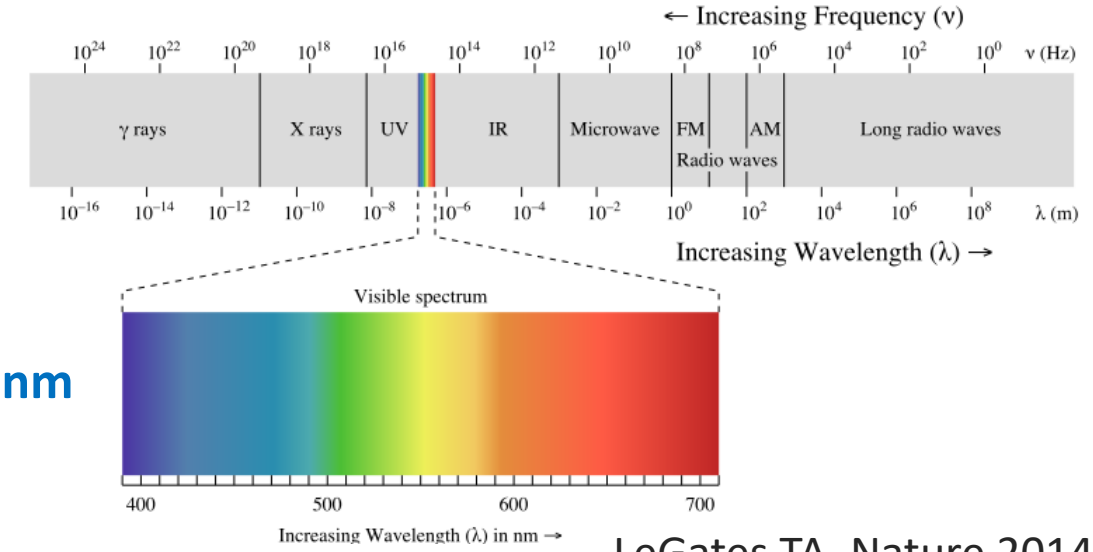
Influences of light on sleep and circadian



ipRGC (M1-5)

non-image forming ganglion cell



Blue light wavelength 460-480 nm

LeGates TA. Nature 2014

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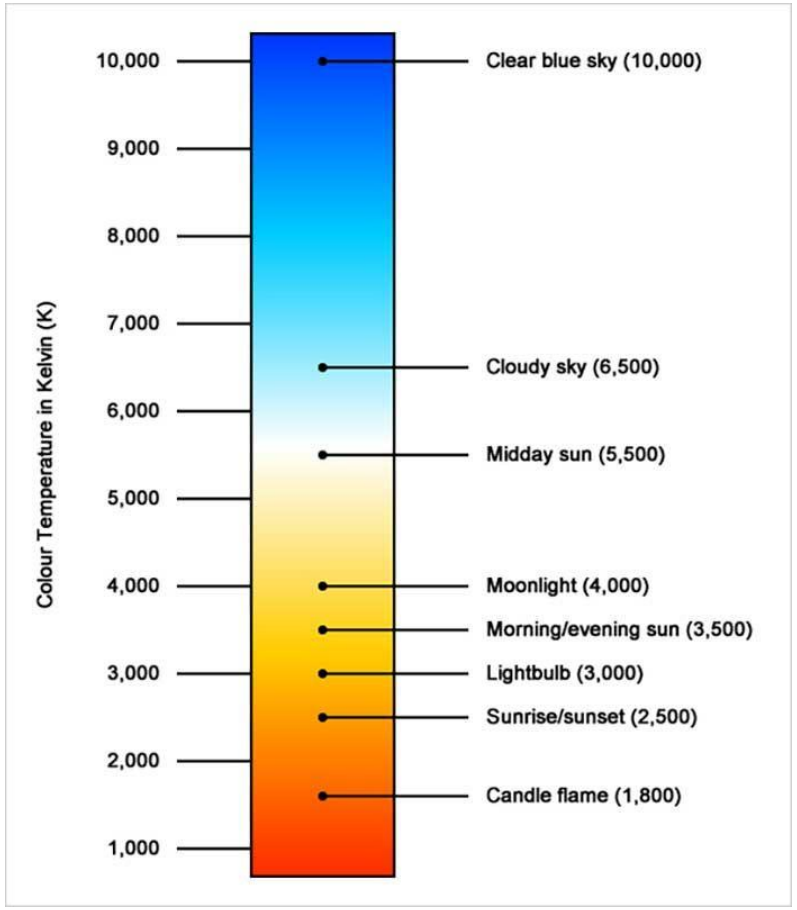
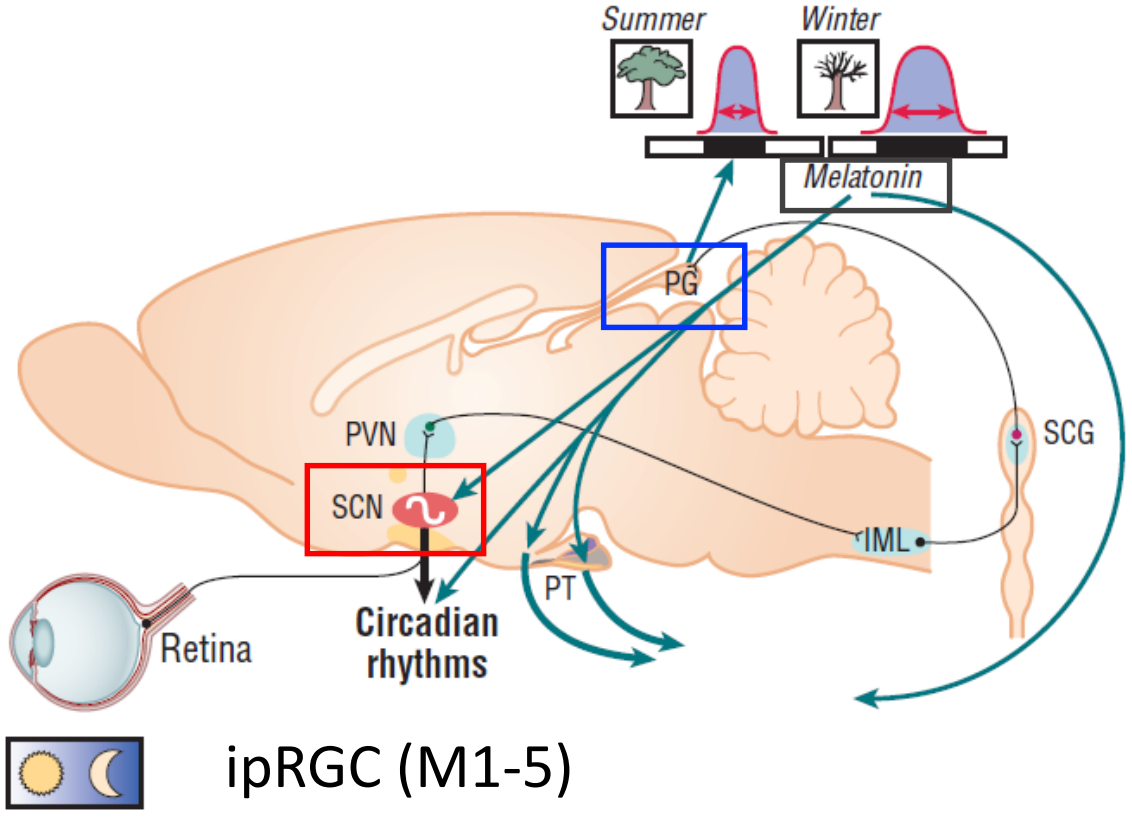
Luminance and color temperature

Iluminance (lux)	Surfaces illuminated by
0.002	Moonless clear night sky with airglow
0.05–0.3	Full moon on a clear night
50	Family living room lights
80	Toilet lighting
100	Very dark overcast day
320–500	Office lighting
400	Sunrise or sunset on a clear day.
1000	Typical TV studio lighting
10,000–25,000	Full daylight (not direct sun)
32,000–100,000	Direct sunlight



LeGates TA. Nature 2014

Effect of light on circadian rhythm: suppression of melatonin



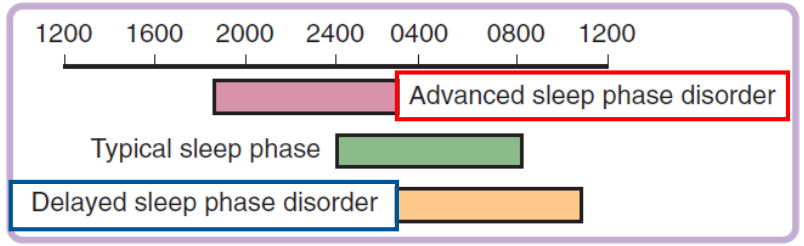
ipRGC (M1-5)

non-image forming ganglion cell

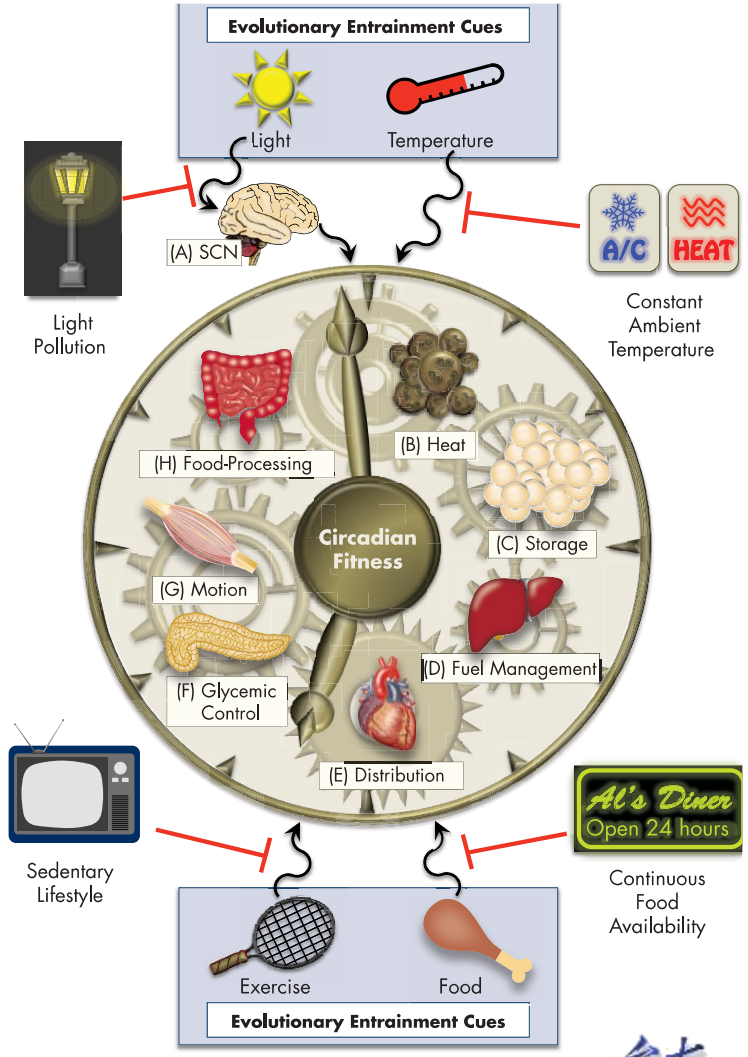
- Body clock: suprachiasmatic nucleus
- Light suppress melatonin secretion
- Melatonin synchronize circadian and seasonal function

SCN: suprachiasmatic nucleus
PG: pineal gland

Impact of environments on circadian: photic and nonphotic zeitgeber

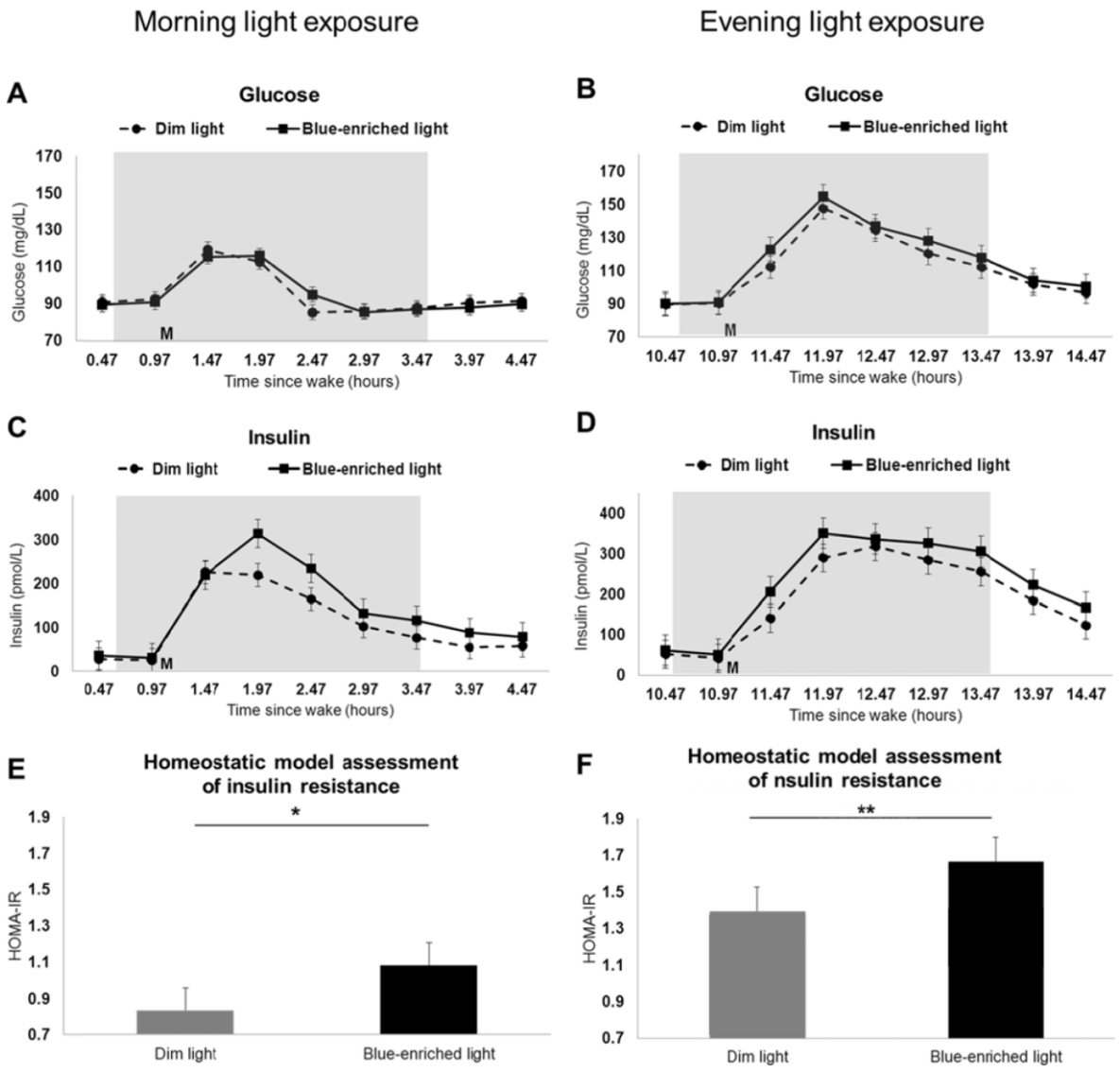


- Cause phase advances
  - Early morning light
  - Exercise during late afternoon or early evening
- Cause phase delays
  - Afternoon light
  - Nocturnal exercise



Gerhart-Hines Endocrine Review 2015

Morning and evening light exposure increase insulin resistance



Cheung IN. PLoS ONE 2016

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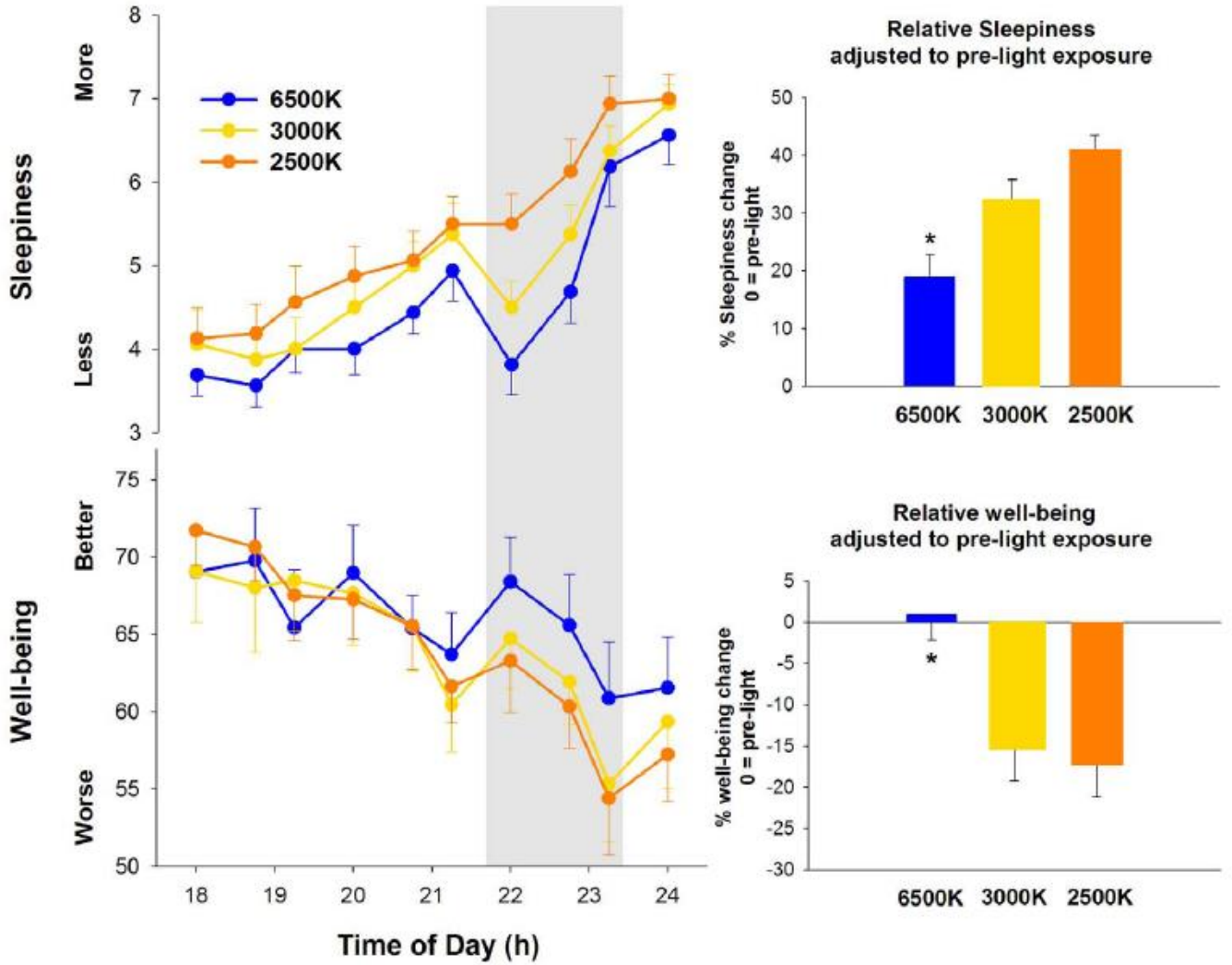
Blue light increase vigilance and reduce sleepiness



Cheung IN. PLoS ONE 2016

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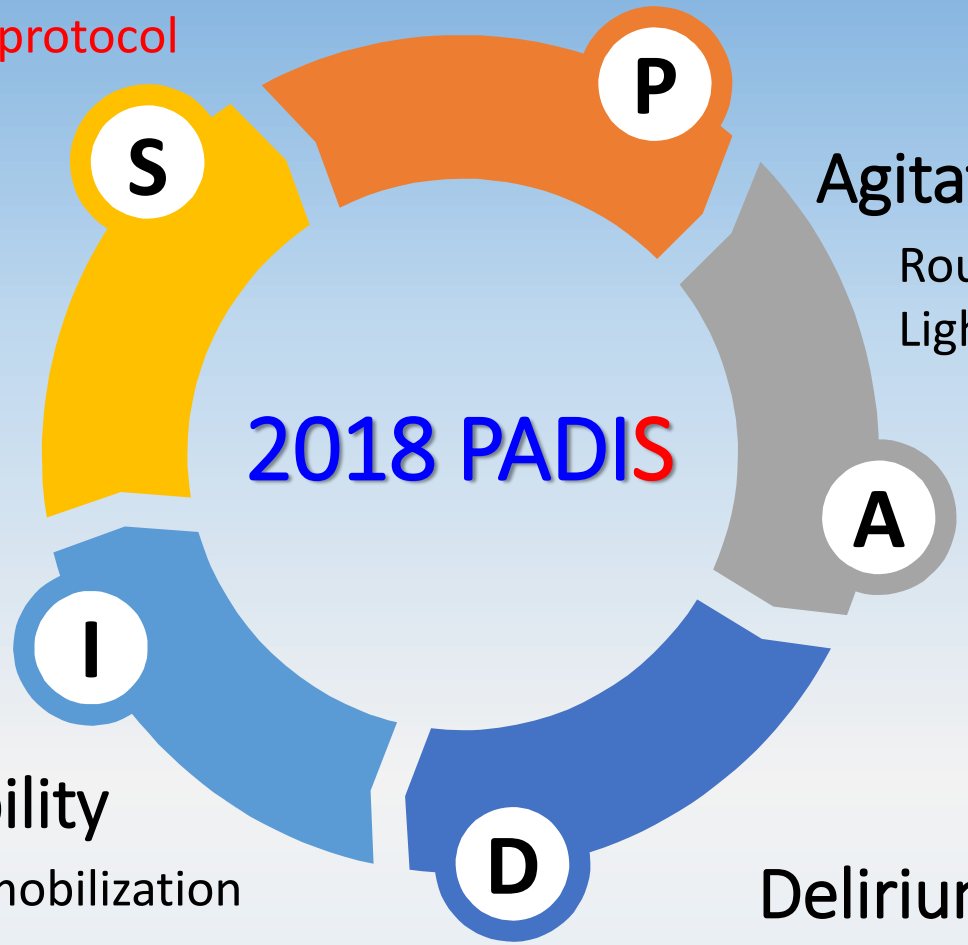
ICU liberation

Pain
Routinely assess
Protocol-based, multimodal

Sleep disruption
Sleep-promoting, multicomponent protocol



Agitation/Sedation
Routinely assess
Light sedation

Immobility
Rehabilitation/mobilization

Delirium
Multicomponent therapy
Dexmedetomidine treat

Main references 1990-2015 October
Discussion updated to 2018

Adapted from PADIS guideline teaching slide

PADIS: Sleep disruption

Sleep Disruption

117

Q29 成人加護病房病人的睡眠特質為何？

Q30 成人加護病房病人睡眠異常的盛行率為何？

Q31 影響睡眠品質的危險因子有哪些？

Q32 睡眠異常是否會影響病人住加護病房時或出加護病房後的臨床結果？

Q33 是否應例行使用生理監測方式來評估病人的睡眠？

Q34 是否應使用非藥物介入措施來改善睡眠？

Q35 是否應該使用藥物來改善睡眠？

Q36 是否應使用促進睡眠流程來改善睡眠？

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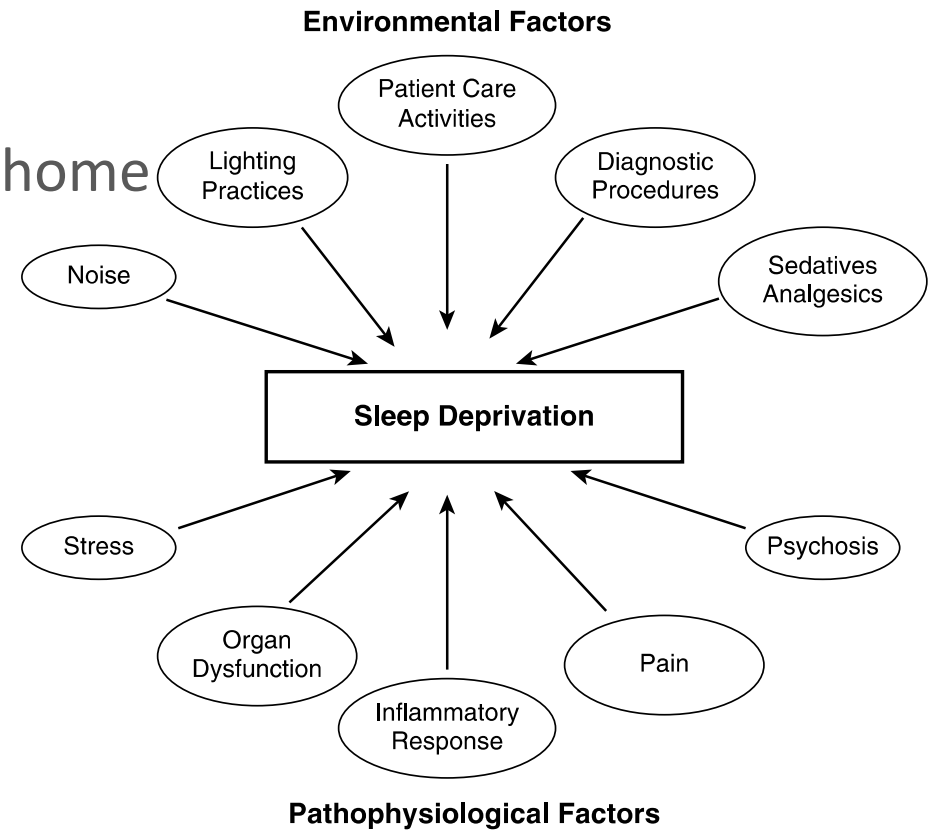
Sleep disruption in critically ill patients

- Characteristic
  - Sleep fragmentation
  - Increased light sleep %(N1+N2) and time spent at sleep at daytime
  - Decreased deep sleep %N3 and %REM
  - Subjective sleep quality reduced
- Presence of delirium
  - May not affect TST, SE, sleep fragmentation
  - %(N1+N2) and %N3 is unknown
  - %REM reduce
  - Increase daytime sleep

Devlin JW. Crit Care Med 2018

Risk factors for sleep disturbance

- Exist before hospitalization
  - Poor-quality sleep
  - Use of a pharmacologic sleep aid at home
- ICU-acquired
  - Pain
  - Environmental stimuli
  - Health care-related interruptions
  - Illness
  - Psychologic factors
  - Respiratory factors
  - Medications



Pisani MA. AJRCCM 2015 ; Devlin JW. Crit Care Med 2018

Impact associated with sleep disturbance and circadian disruption

- Proposed impact associated with sleep deprivation
  - Emotional distress
  - ICU delirium
  - Deranged immune function?
  - Neurocognitive dysfunction?
  - Mortality?
  - Prolonged MV?
  - ICU LOS?

Clinical practices to promote sleep in the ICU

- Self-administered survey from 522 ICU in 10 Eropean countries
- Characters perceived as sleep
  - Lying quietly with closed eye; decreased BP; slow and regular respiration
- 9% had a protocol for sleep management and 1% sleep questionnaire, especially in central Europe
- Non-pharmacologic sleep-promoting intervention
  - Most common: reduce staff noise; turn room light off; reduce nurse interventions at night; keep patient awake during the day
  - Ear plugs in 18%; 37% reduced ventilator alarm volume

Hofhuis JG. International Journal of Nursing Studies 2018

Sleep disturbance: Actionable patient intervention

Question	Recommendation	Strength	Evidence
Routine physiologic monitoring	Not	conditional	very low
AC ventilation (vs PS) used at night	Yes	conditional	low
Adaptive mode ventilation at night	No recommendation	none	very low
NIV-dedicated ventilation (vs standard ICU ventilation with NIV capacity)	Either NIV-dedicated ventilator or standard ICU ventilatory	conditional	very low
Aromatherapy, acupressure, music at night	Not	conditional	low; very low
Noise or light reduction strategy used at night	Yes	conditional	low
Sleep-promoting medication (melatonin, dexmedetomidine, Propofol)(vs no use)	No recommendation for melatonin and dexmedetomidine Not using propofol	none conditional	very low; low low
Sleep-promoting protocol	Yes	conditional	Very low

Devlin JW. Crit Care Med 2018

Sleep assessment: routine physiologic monitoring? Lack of evidence!

Remarks:

- Physiologic monitoring: actigraphy, bispectral (BIS) analysis, EEG and/or PSG
- NOT include monitoring a patients' perceived sleep by either validated assessment (e.g. Richard-Campbell Sleep Questionnaire) or informal subjective bedside assessment.

Rationale:

None of the 5 critical outcomes (i.e. delirium occurrence, duration of MV, ICU LOS, ICU mortality, and patient satisfaction) for this question have been studied.

Recommendation:

Routinely using physiologic sleep monitoring clinically in critically ill adults is not suggested (conditional recommendation, very low quality of evidence)

Adapted from PADIS guideline teaching slide

Society of Critical Care Medicine
The Intensive Care Professionals
Right Care Right Now.

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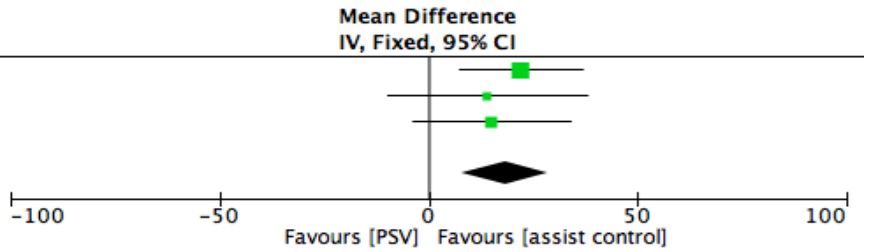
Assist control vs. PS mode at night

- Sleep efficiency increased by 18.33% (95% CI, 7.89-28.76)

Study or Subgroup	Control Ventilation Mean	SD	Total	PSV Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Andrejak 2013	61	25	26	39	29	26	50.3%	22.00 [7.28, 36.72]
Cabello 2008	58	28.2	15	44	37.8	15	19.1%	14.00 [-9.87, 37.87]
Toublanc 2007	65	25	20	50	35	20	30.6%	15.00 [-3.85, 33.85]
Total (95% CI)			**61**			**61**	**100.0%**	**18.33 [7.89, 28.76]**

Heterogeneity: $Chi^2 = 0.49$, $df = 2$ ($P = 0.78$); $I^2 = 0\%$
Test for overall effect: $Z = 3.44$ ($P = 0.0006$)



- %REM: increase by 2.79% (95% CI, 0.53-5.05)
- Change in % N2 not significant, by 0.31% (95%CI, -5.17-5.79)
- Change in % N1 not significant, by 5.29% (-4.38-14.97)

Adapted from PADIS guideline teaching slide

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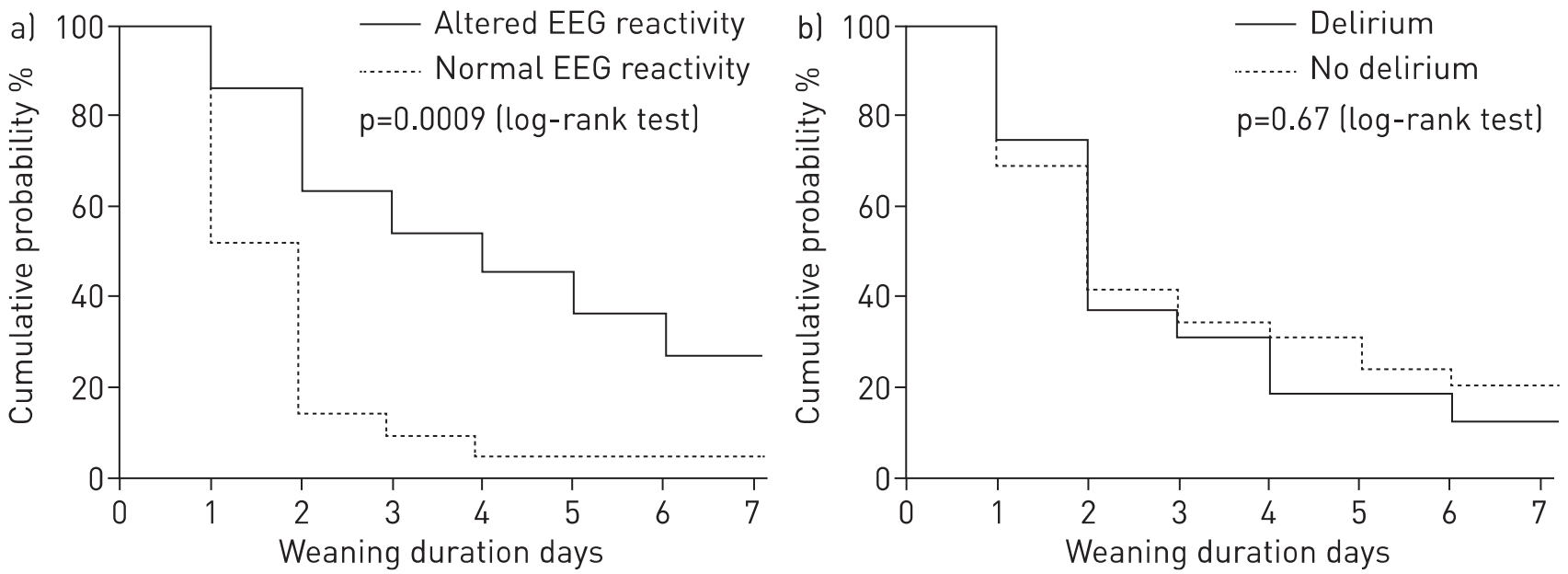
Impact of sleep alterations on weaning duration

- 24 hr PSG monitoring
- Subject: intubation >24 and ≥1 SBT fail



- Median MV duration: normal sleep 5 day, atypical sleep 13 day

Thille AW. Eur Respir J. 2018

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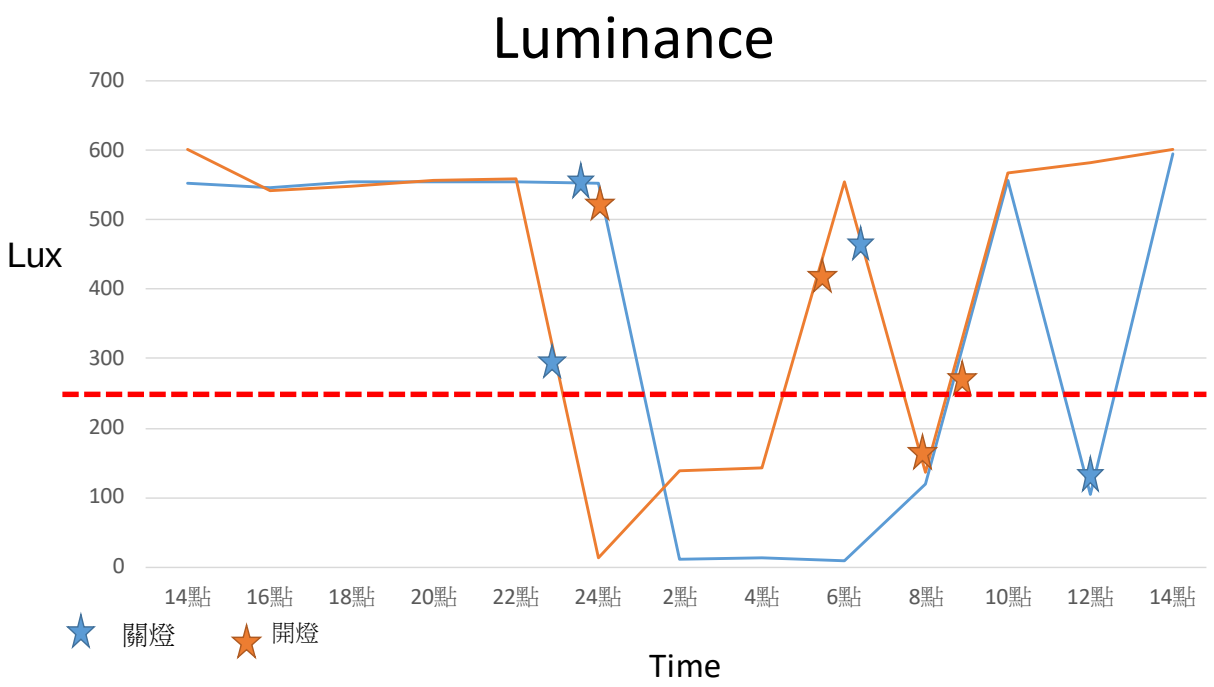
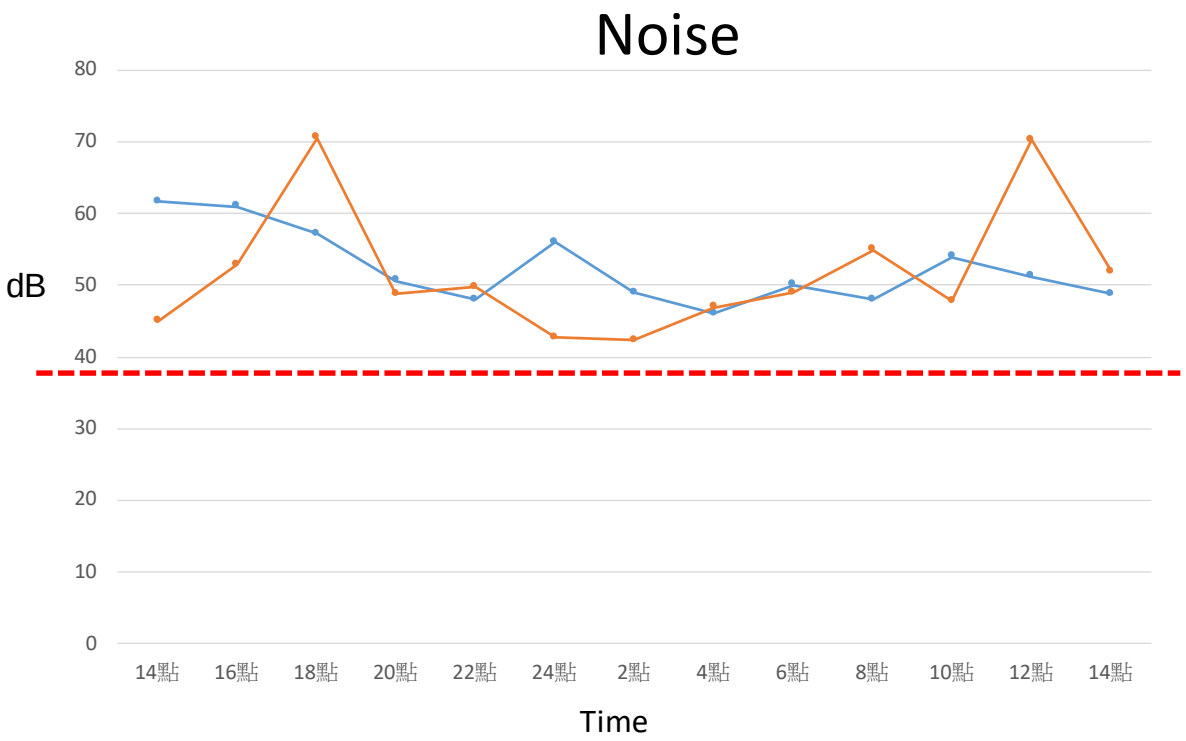
Luminance and noise in 24hr





ECMO　stable and awake patient　sleep center with light fully on

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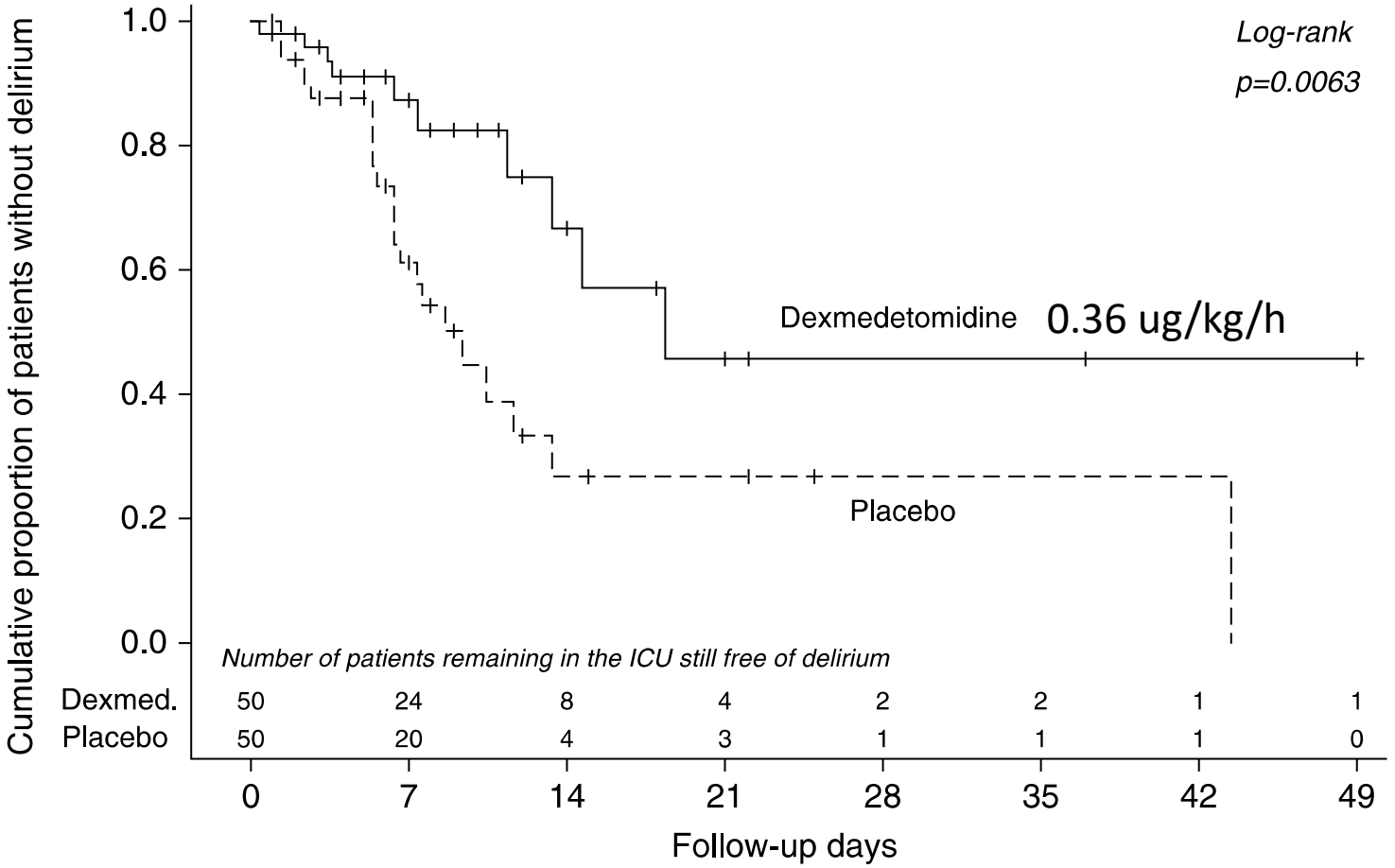
Dexmedetomidine reduce delirium but not change sleep perception



No difference in daily Leeds Sleep Evaluation Questionnaire

Skrobik Y. Am J Respir Crit Care Med 2018

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Selection of hypnotics for patients with respiratory insufficiency

Class	Drugs	Mechanism of Action	Sleep Architecture
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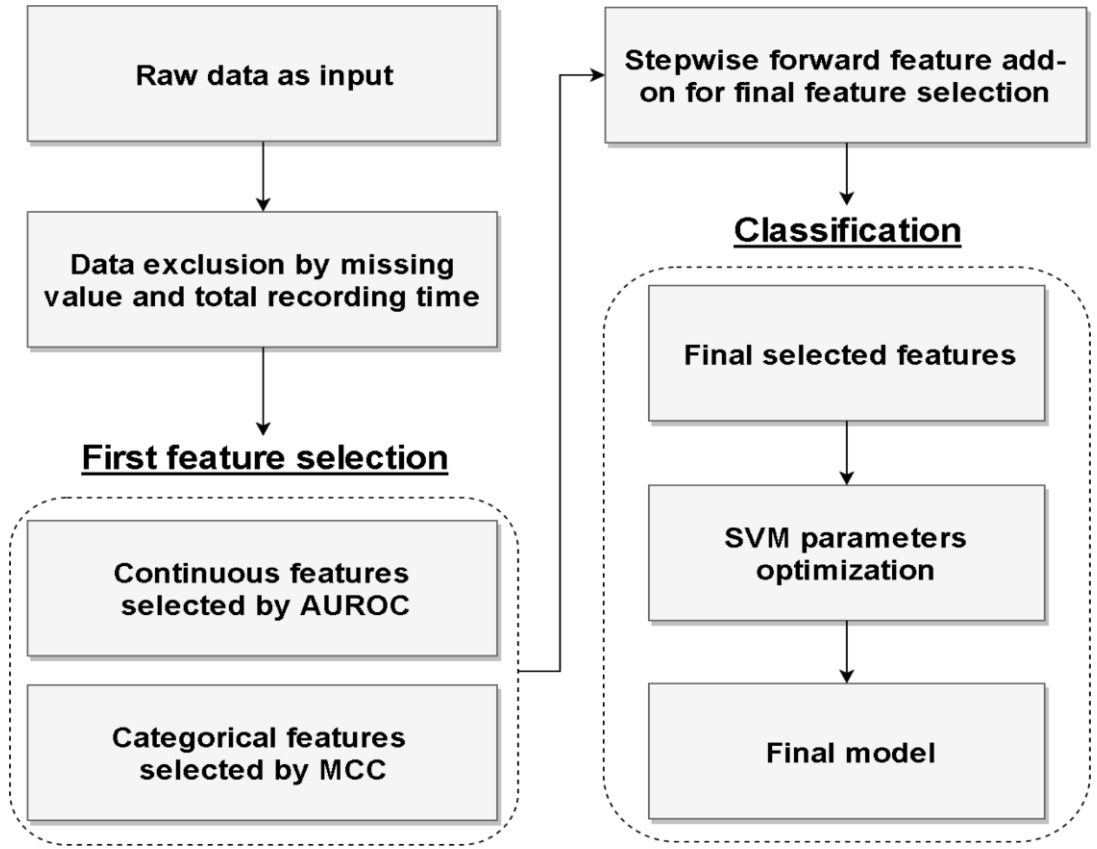
Jamil SM. AnnalsATS 2017, Forshew DA. Amyotroph Lateral Scler Other Motor Neuron Disord. 2003

Proposed future research

- How to improve the understanding of nature of sleep and circadian and highlight the awareness for ICU staff
- Association between intrinsic chronotype and sleep disturbance
- Solution for lack of impact of routine physiologic monitoring
  - Identify target outcomes other than traditional ICU outcomes
  - Combination of subjective and objective measurement of sleep disturbance and circadian disruption
    - Chinese version of candidate questionnaire (LESQ, RCSQ) *plus* actiwatch +/- minimal EEG channel for measurement of sleep
- Data mining of the big data collected in the intelligence ICU to compliment expertise care with artificial intelligence

Example: Support vector machine prediction of OSA in a large-scale clinical sample

- A large-scale sleep lab based dataset (n=6875)
  - Features commonly collected at outpatient clinic
- Aim to to develop a SVM-based prediction model to identify patients with high probability of OSA for non-sleep specialist physician in clinical practice



Huang YC & Lee PL. SLEEP 2019 in Press

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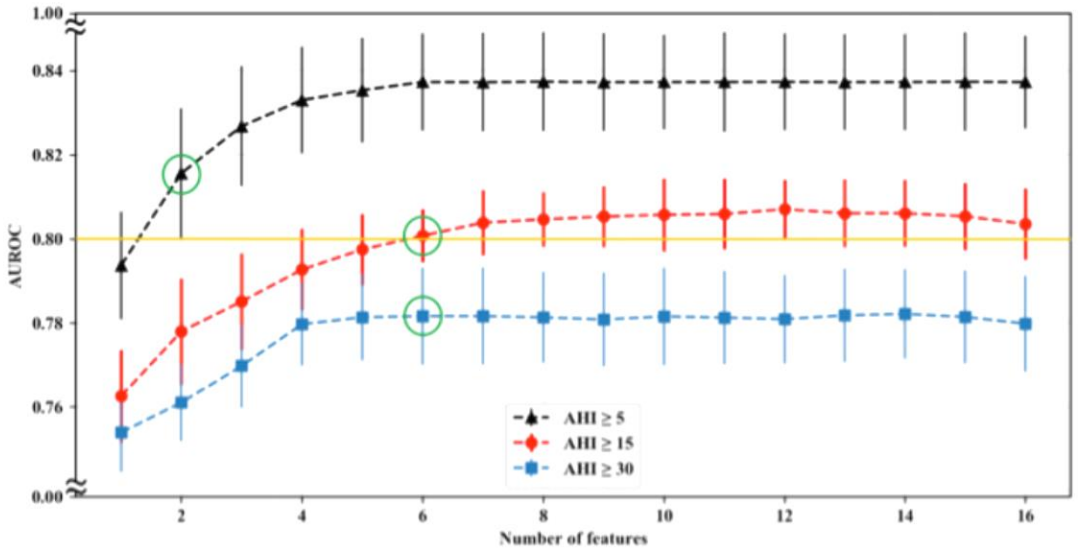
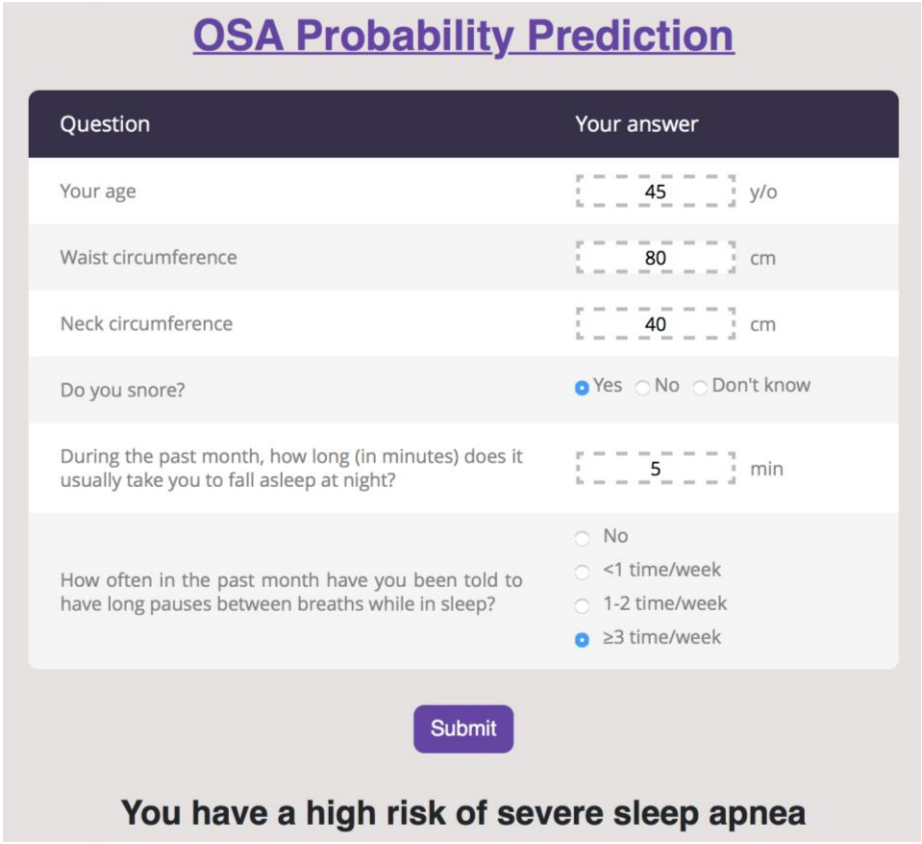
Selected features and predictability

- Feature number: AHI ≥5 /h: 2, ≥15/h: 6, and ≥30/h: 6



- AUROC, Sen, and Spe higher than BQ and NoSAS

- http://howareyou.csie.ntu.edu.tw



Huang YC & Lee PL. SLEEP 2019 in Press

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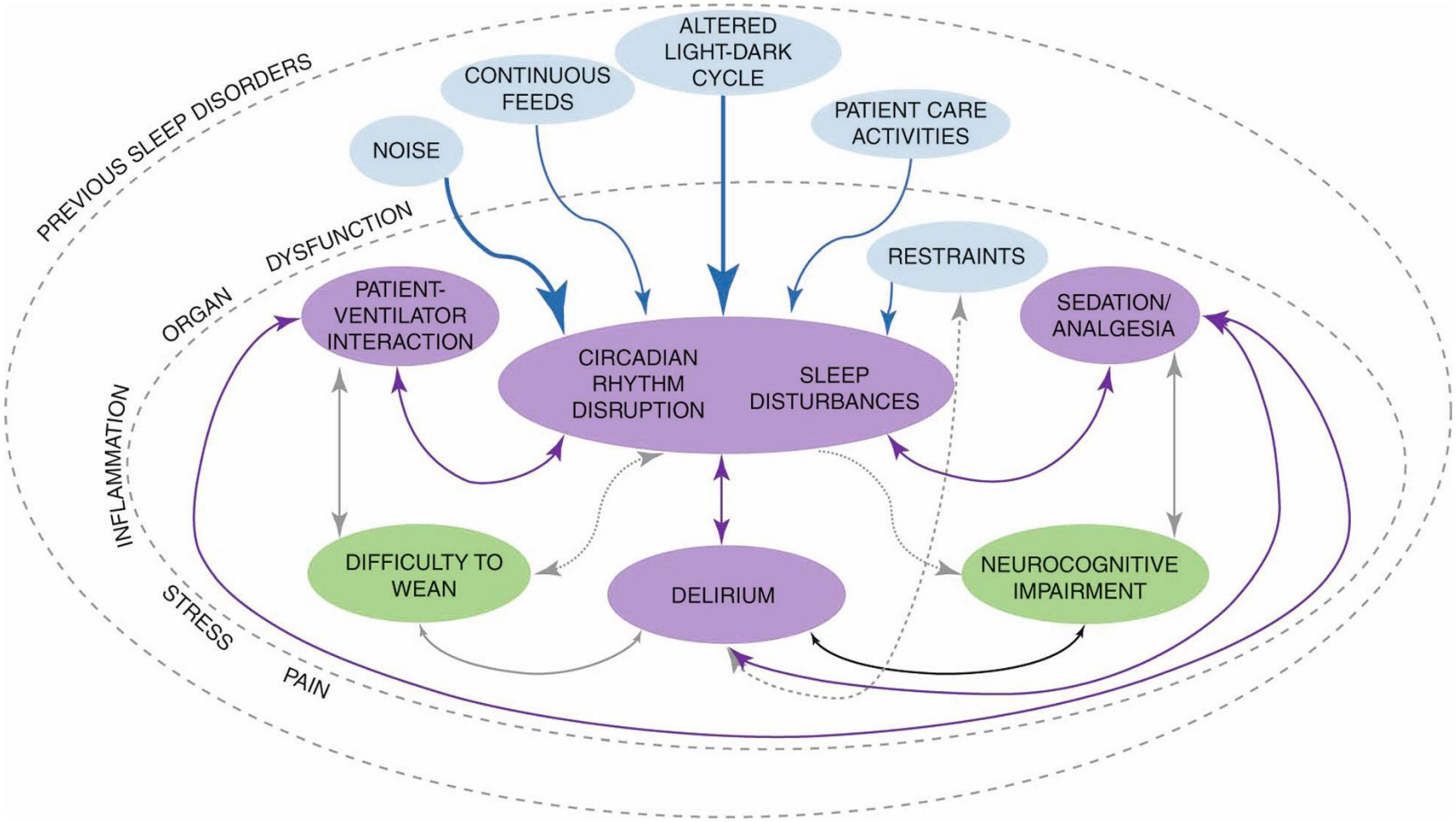
Summary



Telias I. Critical Care 2019

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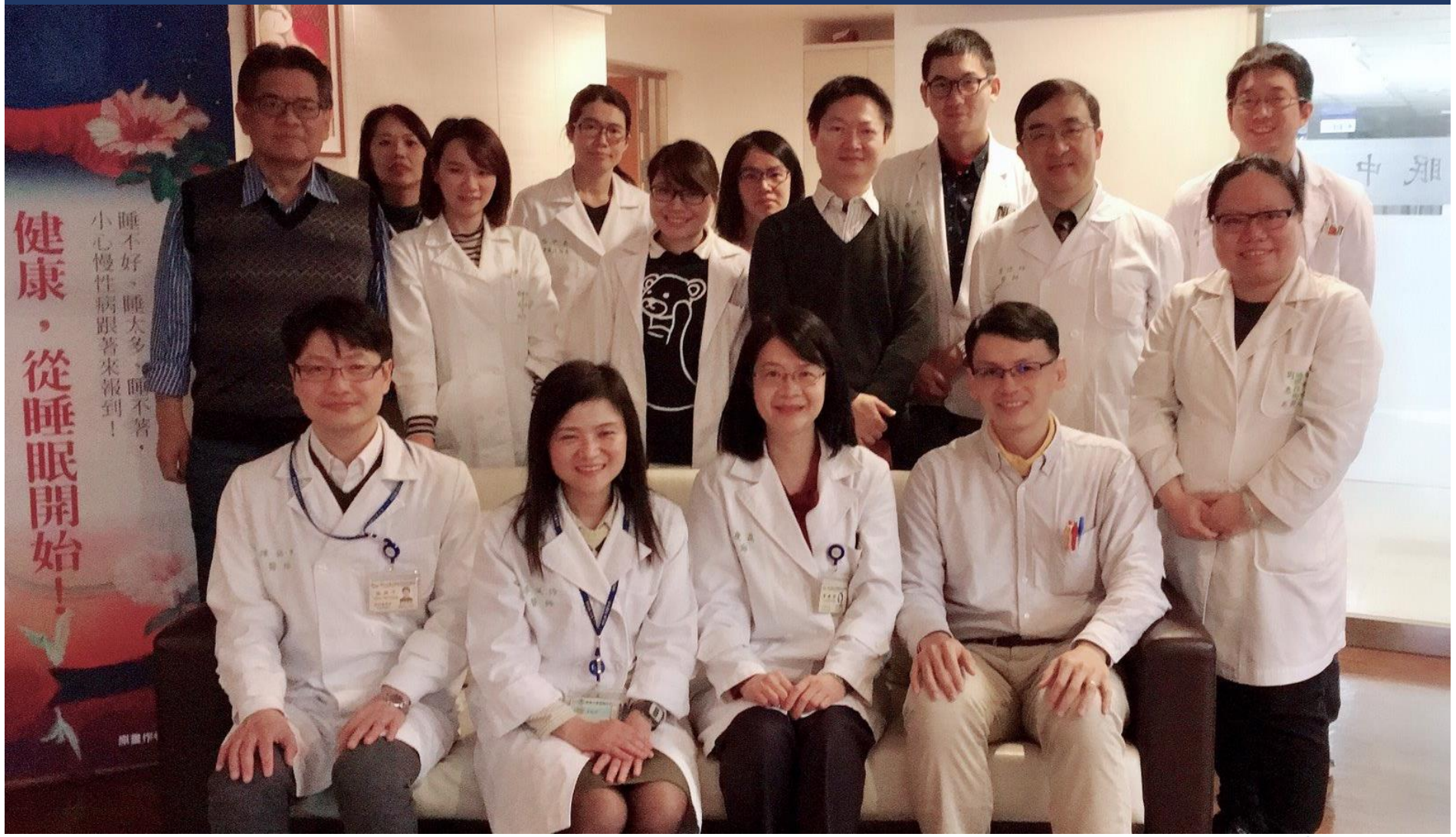
Acknowledgement



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Sleep monitoring: polysomnography

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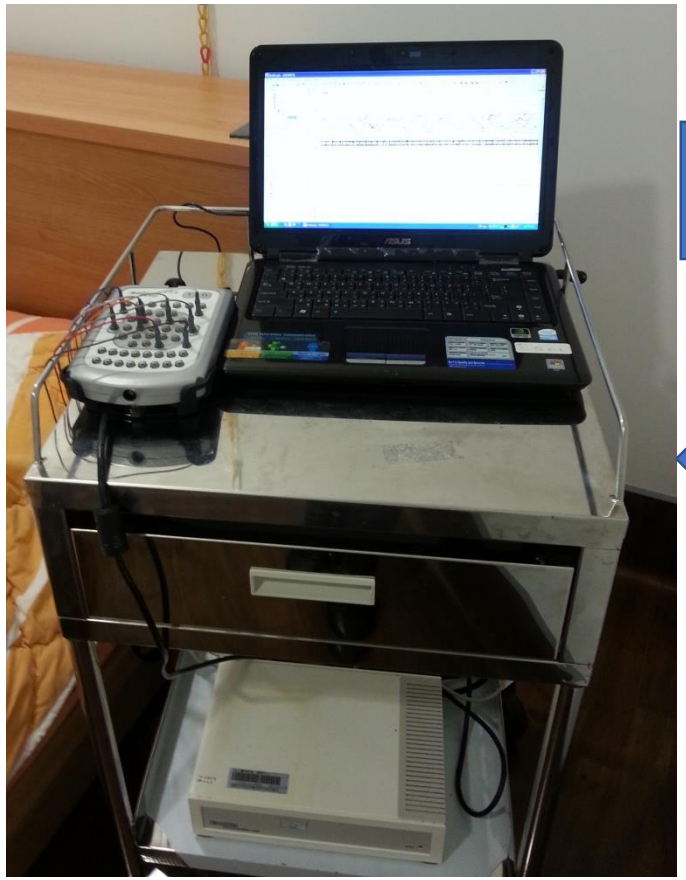
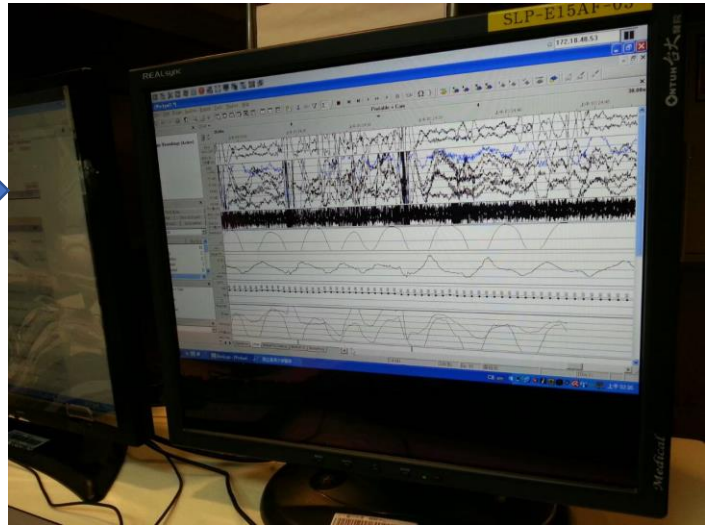
Telemedicine for bedside sleep monitoring

Bedside



Sleep center



Sleep Monitoring

PPV titration

- Signal transmission via Wifi or Bluetooth

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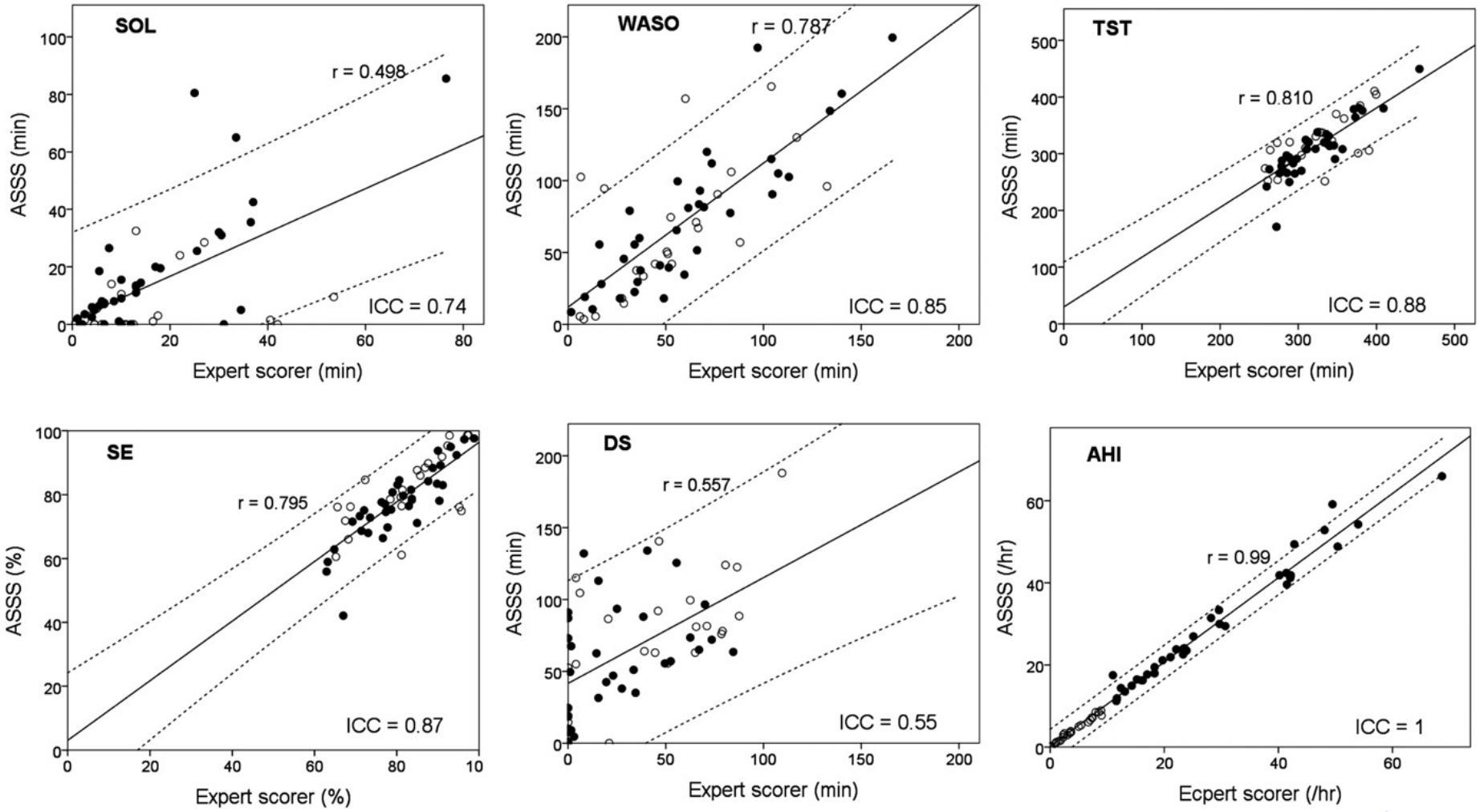
Scatter plots visualizing the concordance between ASSS expert scoring



- ● OSA
- ○ Non-OSA

Lee PL. J Clinical Sleep Med 2019

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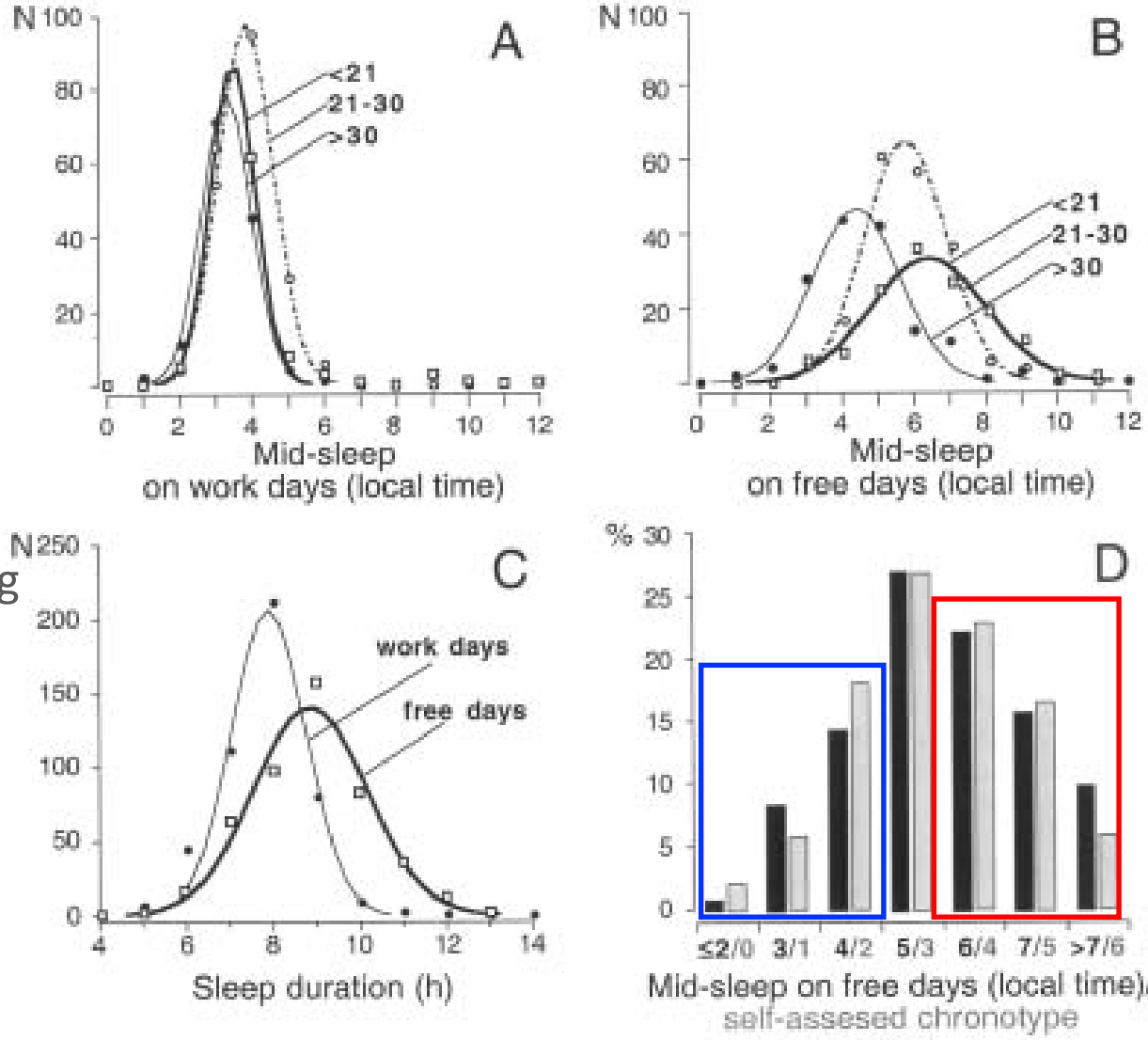
Midsleep phase, sleep duration, and chronotype at adolescent, you adult, and adult

- Midsleep
  - Bedtime + sleep onset + sleep duration/2
    - Weekday: W1-4, W7 night (MSF)
    - Free day: W5-6 night (MSW)
- Social jet lag=MSF- MSW
  - 21-30 y/o has higher social jet lag than <21 y/o and >30 y/o



Roenneberg T. Journal of Biological Rhythm 2003

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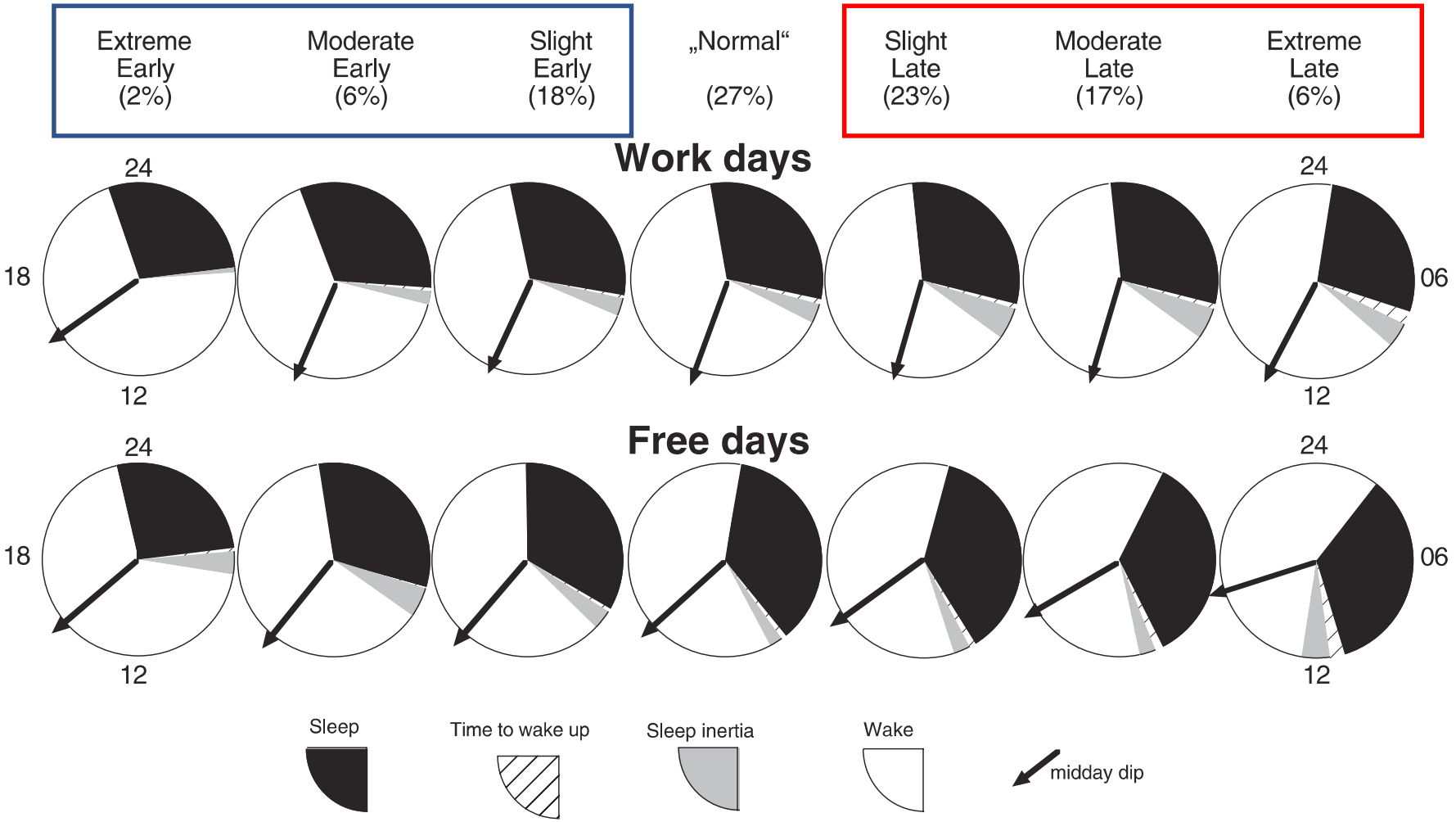
Average day of different chronotypes on workdays and free days: sleep inertia



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