

Monitoring de l'analgésie en peropératoire



Conflits intérêt:

Consultant Fresenius Kabi

Reçu matériel de Metrodoloris, Idmed

Luc Barvais, MD PhD

lbarvais@ulb.ac.be

Université Libre Bruxelles, Belgique

Mesure de la balance NAN

Noci-AntiNociception



Nociception

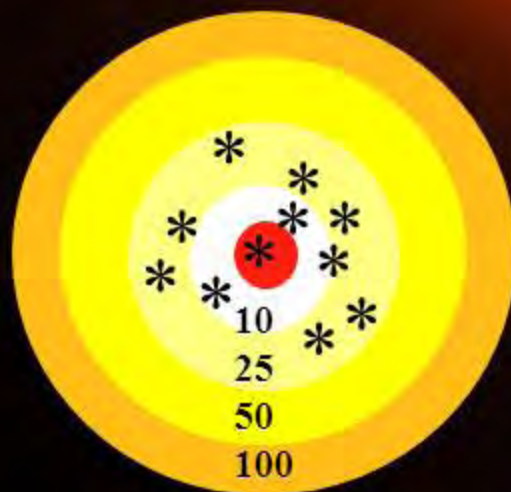


Anti - nociception

Détection inconsciente d'un stimulus douloureux détecté par l'organisme avec réponse SNA (HTA, $\uparrow$ RC), mvt

Comment mesurer l'analgésie perop.?

- Pas de mesure concentration Suf, Fent, Remif!
- Concentration calculée Suf et Remif (Modèle PHC) avec erreur $\approx \pm 30\%$ (comme Diprifusor)

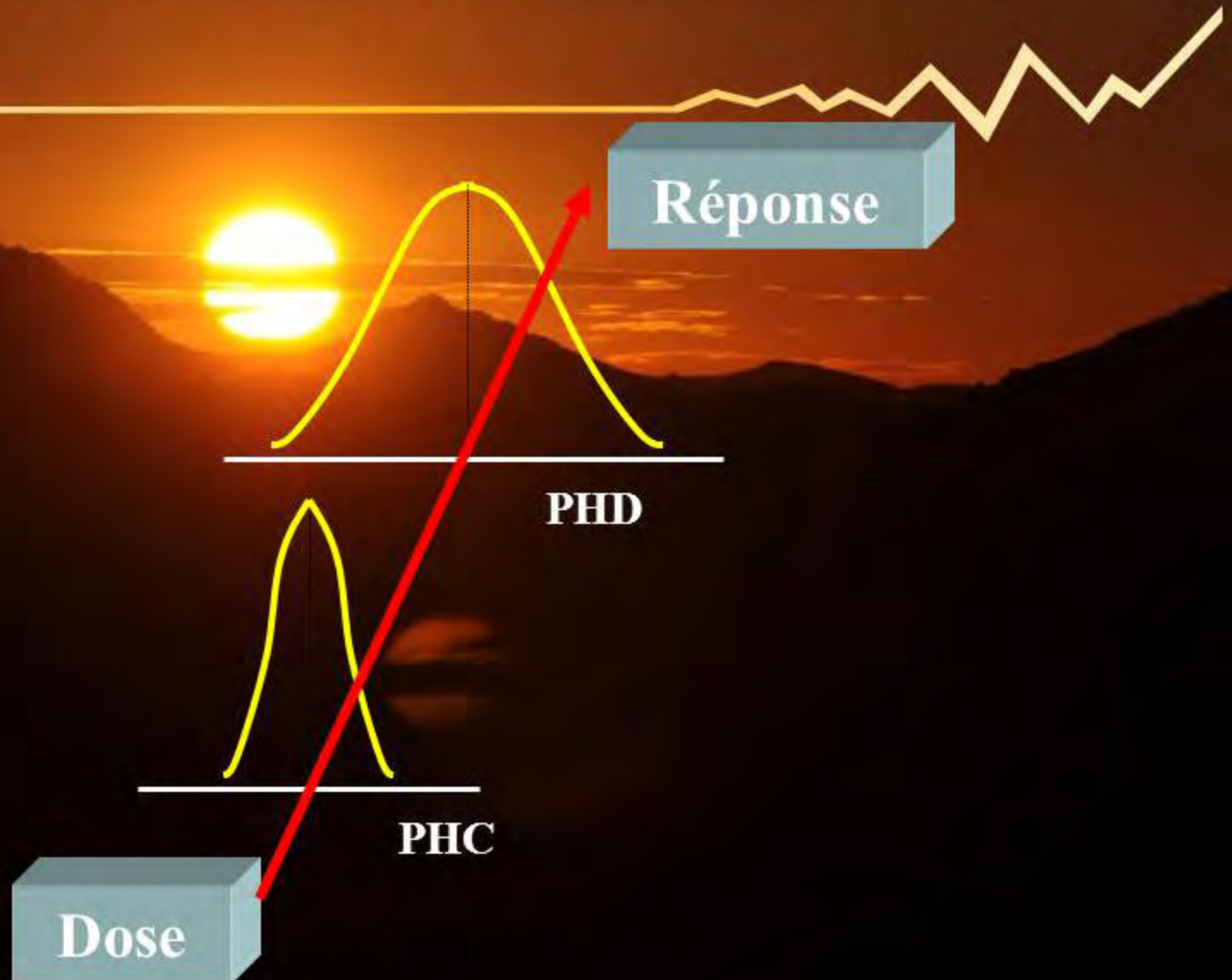


	MDPE	MDAPE	Auteur
Propofol	- 7 %	18.2 %	Marsh
Sufentanil	- 10 %	20.7 %	Gepts
Fentanyl	- 4 %	21 %	Mac Clain
Alfentanil	+ 1 %	17 %	Scott
Remifentanyl	+ 1 %	19 %	Minto

Systeme AIVOC (Ce)



Variabilité interindividuelle

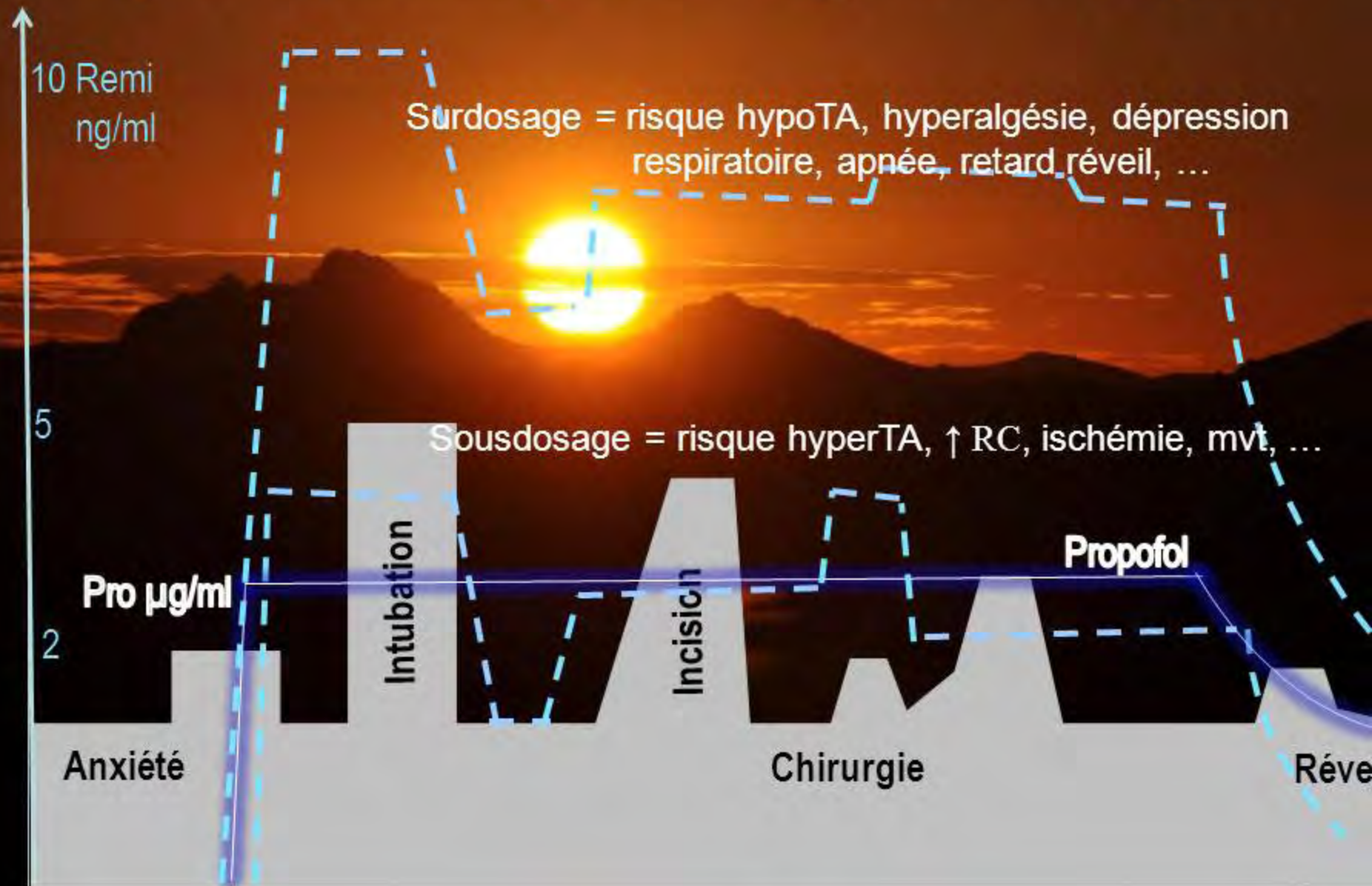


Variabilité PHD interindividuelle

The background of the slide features a warm-toned sunset or sunrise over a range of dark, silhouetted mountains. A bright sun is positioned centrally above the horizon, casting a glow across the sky. Overlaid on the upper right portion of the image is a white line graph. The graph begins with a horizontal segment on the left, followed by a series of sharp, irregular peaks and valleys, and concludes with a steep upward slope on the far right.

- **> 500%**
- **Multi facteurs:**
 - **Génétique**
 - **Age (↘ DC, ↘ distrib., ↘ Vc, ↘ substrat neuronal)**
 - **Dysfonction organique (foie, rein, ...)**
 - **Comédication**

Conséquences cliniques analgésie inadaptée



Quel monitoring de la balance NAN?



- **Pression artérielle**
- **EEG**
- **SPI = Index pléthysmographique**
- **Variabilité du RC (AND)**
- **Pupillométrie**

Closed-loop of mean arterial blood pressure during surgery with alfentanil

	Avant chirurgie	Pendant chirurgie
Alf Closed Loop (% of time)	98.9 ± 1.5	95.5 ± 4.3
ET Isoflurane	0.78 ± 0.1	0.86 ± 0.1
Cp Alf (ng/ml)	122 ± 35	181 ± 58
MDPE MAP (%)	4.2 ± 6.2	8.8 ± 9.4
MDAPE MAP %	7.9 ± 3.8	11.8 ± 6.3

Closed-loop of mean arterial blood pressure during surgery with alfentanil



- **Semble optimiser dosage peropératoire alfentanil**
- **Mais quid si patient:**
 - **Hypovolémie**
 - **Drogues vasoactives**
 - ...

Hémodynamique = signe anesthésie inadéquate

Quel monitoring de la balance NAN?

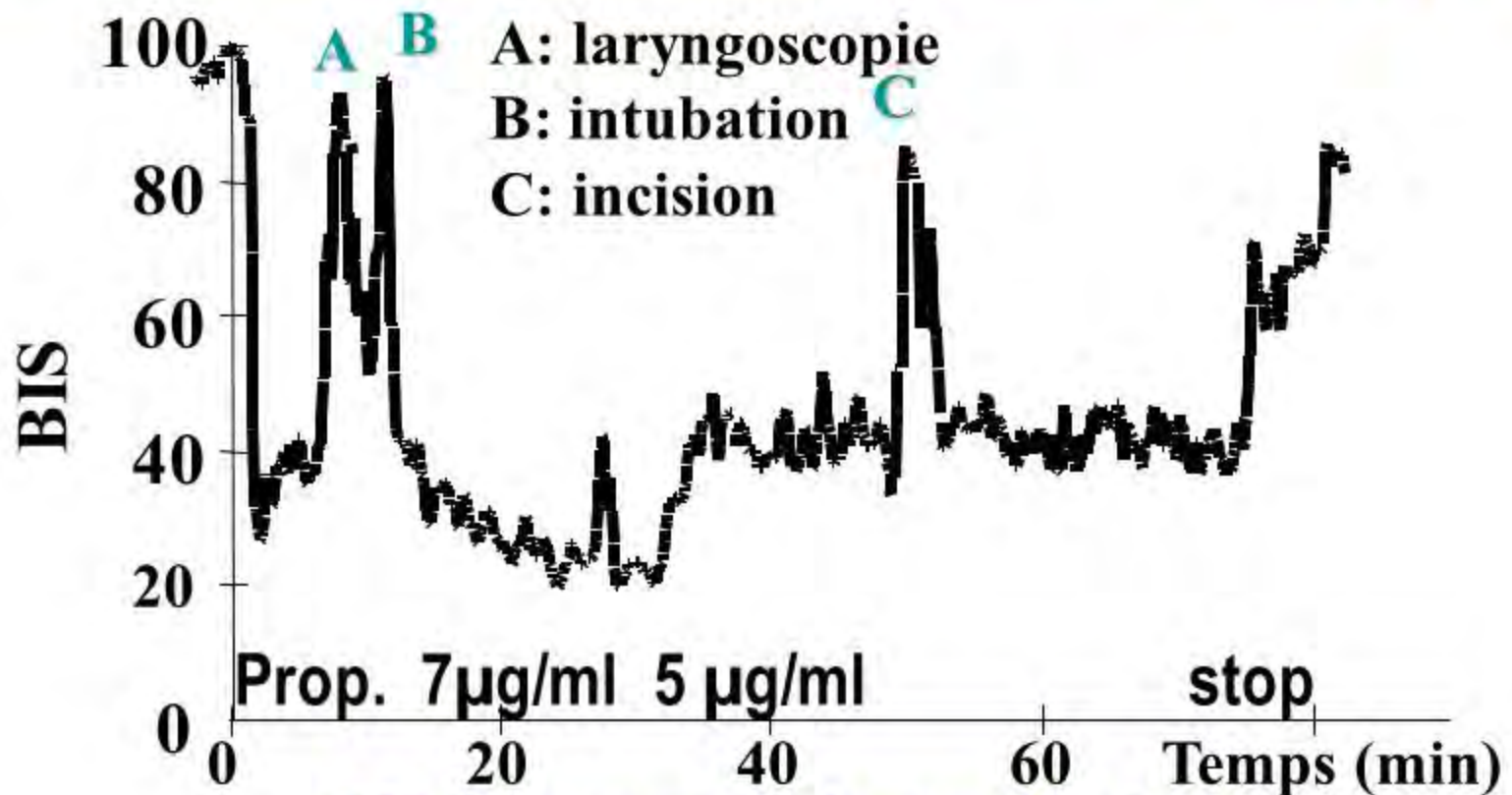


➤ Pression artérielle

➤ **EEG**



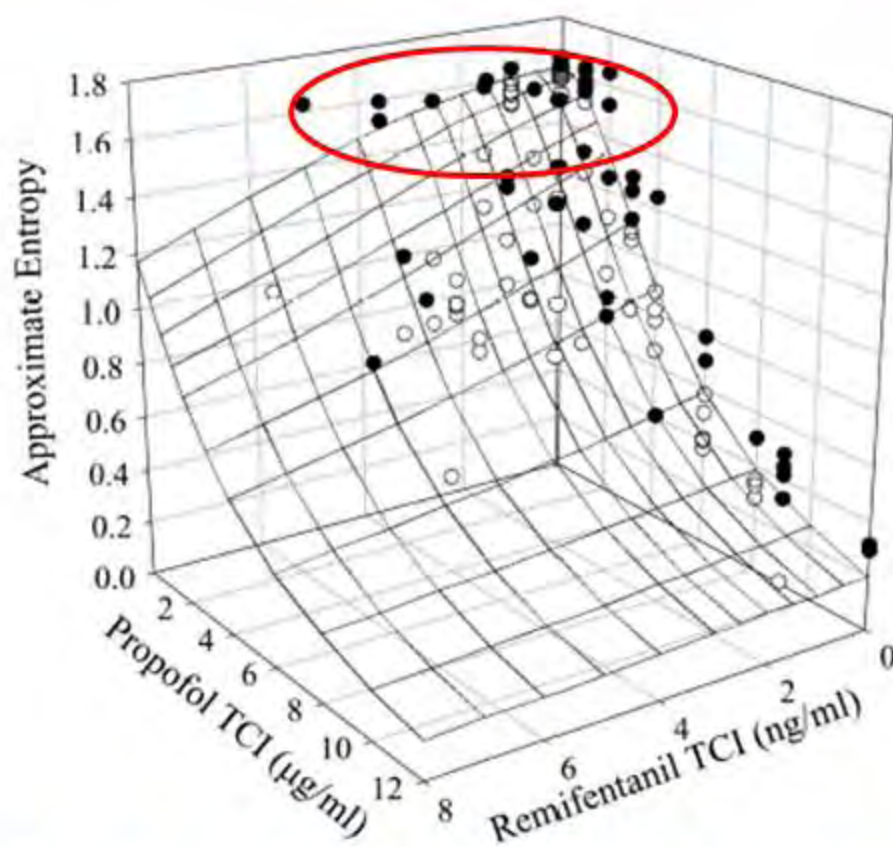
EEG et réaction à la douleur



BIS augmente après un stimulus

nociceptif si l'analgésie est inadéquate

EEG & remifentanyl



Bouillon et al., Anesthesiology 2004

Propofol and Remifentanil Differentially Modulate Frontal Electroencephalographic Activity

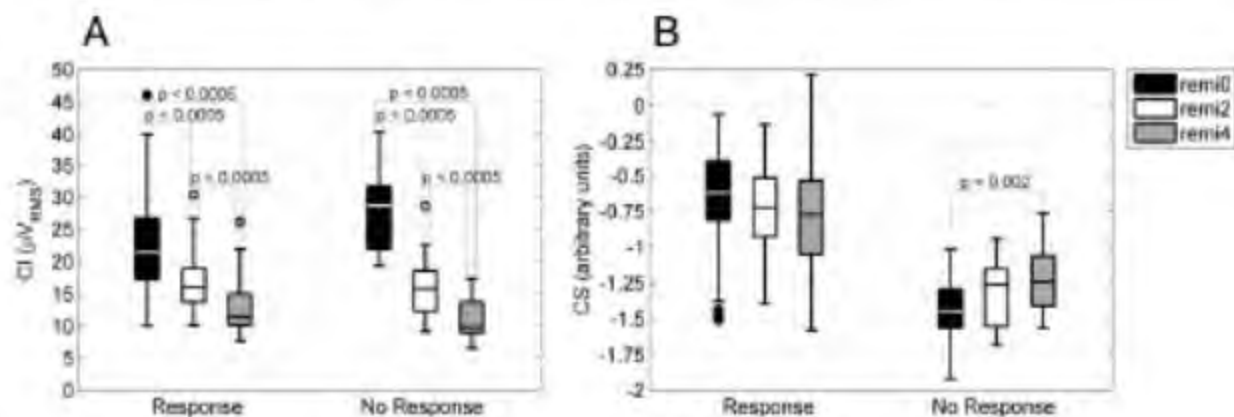
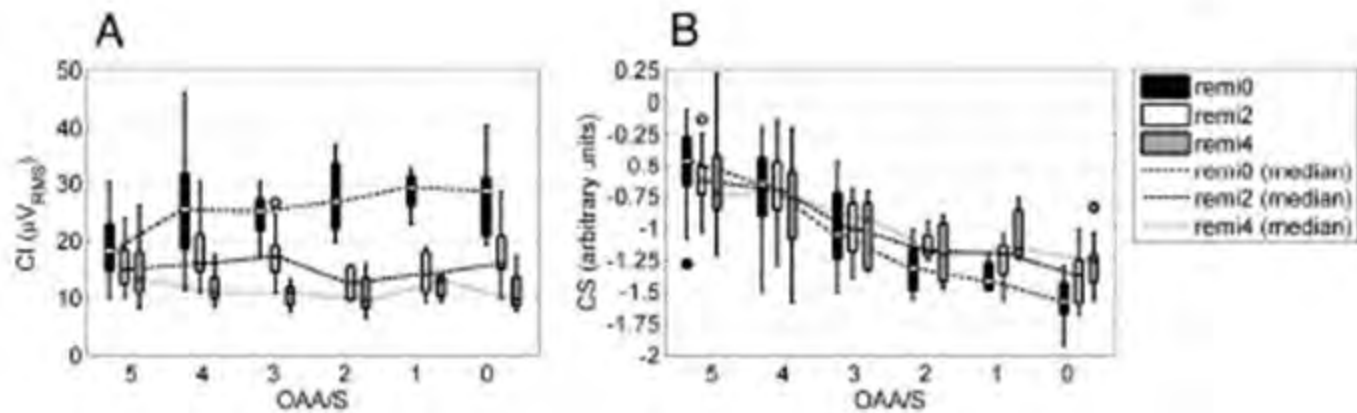
David T. J. Liley, M.B., Ch.B., Ph.D.,*

Nicholas C. Sinclair, B.Sc. (Medical Biophysics), B.E. (Electrical and Electronic) (Hons),†

Tarmo Lipping, Dr.Tech.,‡ Bjorn Heyse, M.D.,§ Hugo E. M. Vereecke, M.D., Ph.D.,||

Michel M. R. F. Struys, M.D., Ph.D.#

- **New mathematical technique for the frontal EEG analysis during propofol-remifentanil TCI**
- **« Fixed order AutoRegressive Moving Average modeling = ARMA**

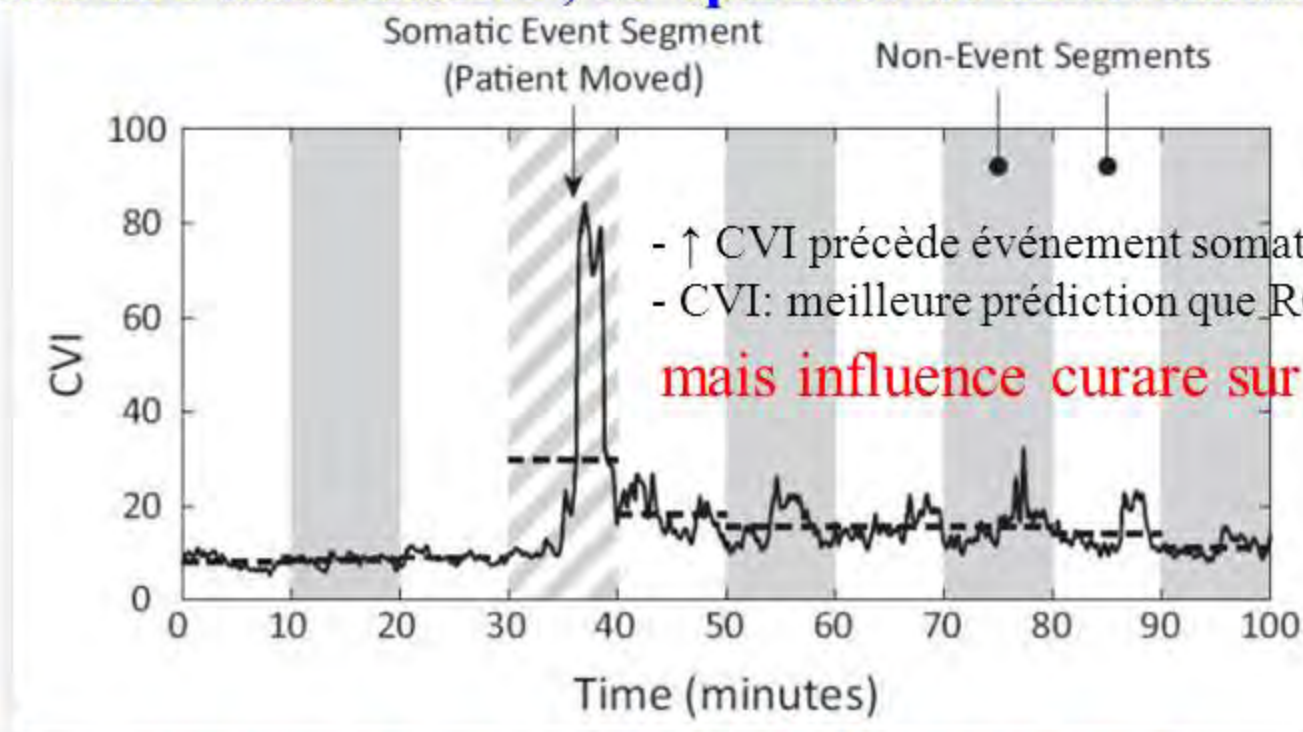


Cortical Input

Cortical State

Increases in EEG and EMG Variability Are Associated with an Increased Incidence of Intraoperative Somatic Response

120 patients; Sevo et propofol ajustés pour cible BIS entre 45-60;
Composite Variability Index = index simple mesurant la variabilité combinée du BIS et EMG
Cliniciens blindés du CVI ; Remifentanyl administré selon la discrétion de l'anesthésiste ; 33 épisodes de mouvements/grimace



Mathews D et al. Anesth Analg 2012;114:759-70

- **EEG et balance NAN :**

- Non invasif et mesure composante hypnotique
- Ne reflète pas le niveau d'antinociception
- Aujourd'hui = mesure anesthésie inadéquate



≠ entre BIS et Entropie



Chirurgie jambe G $\rightarrow$ $\uparrow$ RE, SE cortex frontal Dr.!



Quel monitoring de la balance NAN?



- Pression artérielle
- EEG
- **SPI = Index pléthysmographique**

Amplitude du pléthysmogramme du doigt

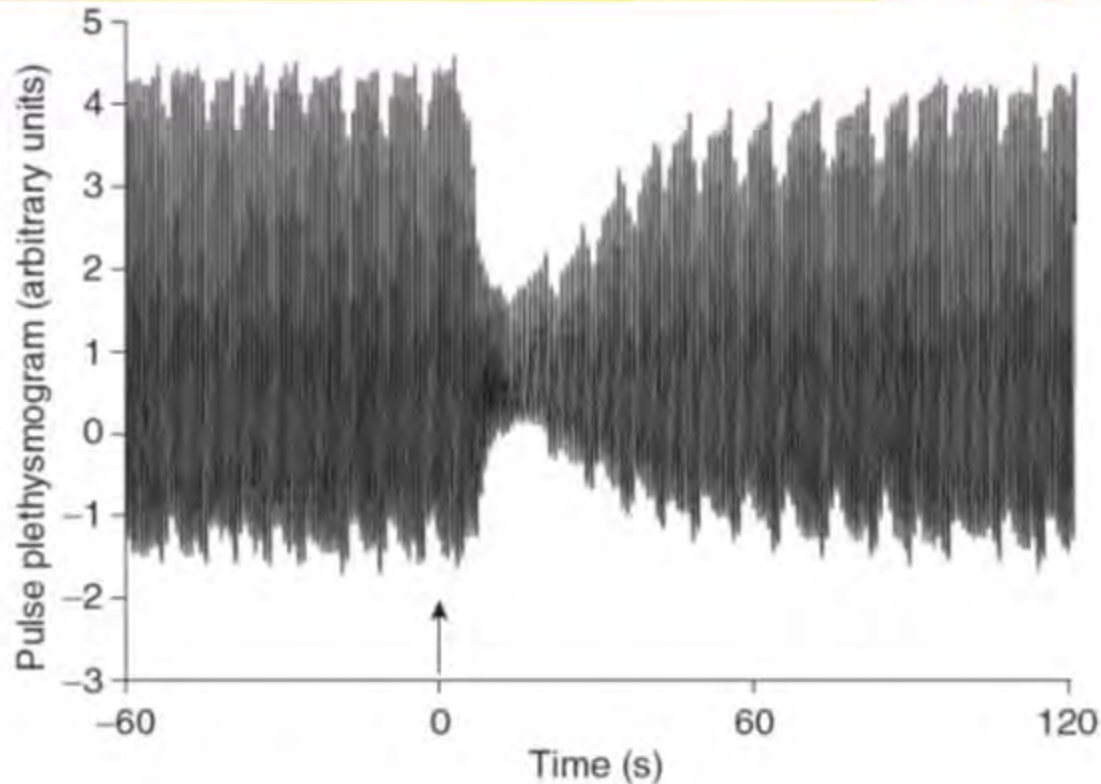


Fig. 1 PPG curve of a typical subject from 60 s before and 120 s after electrical stimulation of the ulnar nerve (arrow).

Luginbühl M et al: Br J Anaesth 2006;96:323-329.

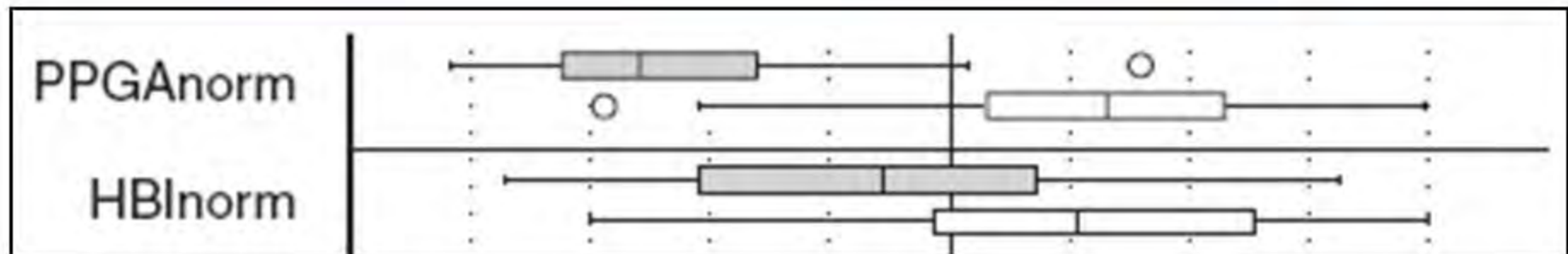
Assessment of surgical stress index during GA

A decorative yellow line graphic that starts as a horizontal line and then continues as a jagged, upward-trending line on the right side of the slide.

Phase Développement index SPI

- 55 patients, 18-60 ans, ASA I-II
- Propofol AIVOC : SE entre 35 et 60 ; Rocuronium
- Remifentanil AIVOC randomisé à incision cutanée et variable pendant la chirurgie à des cibles de 1, 3, 5 ng/ml

Assessment of surgical stress index during GA



Correlation coefficient

— with stimulus intensity
+ with remifentanil Ce

$$\text{SPI} = 100 - (0,7 \times \text{PPGAnorm} + 0,3 \times \text{HBInorm})$$

SPI = Index pléthysmographique



Cible = intervalle 20-50

Influence of different remifentanil concentrations on the performance of the SPI to detect a standardized painful stimulus during sevoflurane anaesthesia

- **24 patients ; remiF 0, 2 et 4 ng/ml (randomisé)**
- **Sevo 0.7 MAC**
- **Tetanos 30 secondes, 60 mamp, 50 Hz**
- **Gradient SPI, HR, SE, RE, BIS, mouvement**

Influence of different remifentanyl concentrations on the performance of the SPI to detect a standardized painful stimulus during sevoflurane anaesthesia

Table 2 Pooled data of SSI, HR, NIAP_{sys}, SE, RE, BIS in the period (60 s) before tetanic stimulation (pre-stimulation) and peak values (120 s) after tetanic stimulation (post-stimulation). Data are median (IQR) and mean (SD). Groups were compared using the Wilcoxon signed-rank test or paired *t*-test. **P*<0.01, ***P*<0.001 vs pre-stimulation. Change in variables is presented as Δ values (post-stimulation–pre-stimulation difference) in subgroups where movement occurred after tetanic stimulation (movers) and no movement occurred after tetanic stimulation (non-movers). Δ Values were compared using the Mann–Whitney *U*-test or unpaired *t*-test, **P*<0.01, ***P*<0.001 vs mover

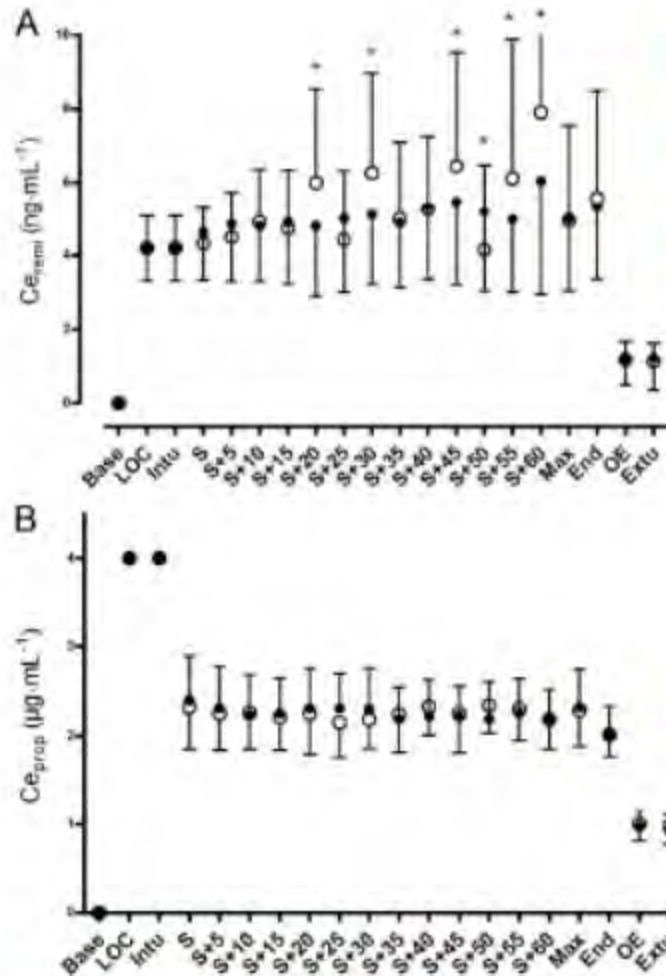
	All pre-stimulation (n=63)	All post-stimulation (n=63)	Movers Δ value (n=20)	Non-movers Δ value (n=43)
SSI	16 (13–20)	29 (18–38)**	20 (16–33)	5 (1–15)**
HR (beats min ⁻¹)	56 (8)	61 (15)**	11 (10)	3 (7)**
NIAP _{sys} (mm Hg)	91 (13)	91 (10)	0 (9)	0 (8)
SE	41 (31–51)	42 (35–53)*	5 (0–11)	2 (–2 to 5)
RE	41 (33–52)	45 (37–55)**	7 (2–14)	2 (–1 to 5)*
RE–SE	1 (0–2)	1 (0–3)	2 (0–7)	0 (0–0)*
BIS	39 (32–49)	43 (35–53)**	3 (0–11)	1 (–1 to 5)

- $\Delta \text{SPI} \geq 10$ = meilleur critère de prédiction du mouvement
- $\text{SPI} = 10 \times$, seul paramètre de détection du tétanos

→ SPI = meilleure variable comparé au BIS, SE, RC, NIBP

Comparison of surgical stress index-guided analgesia with standard clinical practice during routine general anaesthesia

- 2 groupes de 40 patients
- Propofol → BIS50 dans chaque groupe
- Remifentanyl AIVOC titré selon:
 - SPI: range 20-50
 - Critères hémodynamiques
(RC <45 or >90 ; TAM <80% ou >120% + mouvement, toux, ...)



Débit perfusion remifentanil :

Groupe contrôle: $12.3 \pm 5.2 \mu\text{g/kg/h}$

Groupe SPI (cercle plein): $9.5 \pm 3.8 \mu\text{g/kg/h}$

$Ce_{propofol} \equiv 2$ groupes

Fig. 2. Changes in predicted effect-site concentrations of remifentanyl (A) and propofol (B) (Ce_{remi} and Ce_{prop} , respectively) in the surgical stress index group (filled circle) or the control group (open circle) at certain time points during anaesthesia: baseline (base), loss of consciousness (LOC), intubation (intu), start of surgery (S), maximum stimulation (max), discontinuation of propofol and remifentanyl (end), eyes opening (OE), and extubation (extu). Values are given as mean (SD); * $P < 0.05$ compared with the control group.

Comparison of surgical stress index-guided analgesia with standard clinical practice during routine general anaesthesia

Table 5. Number of Unwanted Events during the Intraoperative Period

	SSI Group (n = 40)	Standard Practice (n = 40)
Hypertension	11 (0.28)*	84 (2.1)
Hypotension	5 (0.13)*	67 (1.68)
Tachycardia	0 (0)	2 (0.05)
Bradycardia	23 (0.57)*	111 (2.78)
Movements	3 (0.08)*	14 (0.35)
Total unwanted events	42 (1.05)*	278 (6.95)

Data are numbers of unwanted events during surgery. Data in parentheses are numbers of unwanted events per patient.

* $P < 0.01$ when compared with standard analgesia practice group.

SSI = surgical stress index.

Sufentanil administration guided by SPI versus standard practice during sevoflurane anaesthesia: a randomized controlled pilot study

- **94 patients randomisés:**
 - **SUF bolus (10 µg) si SPI > 50**
 - **SUF bolus selon paramètres hémodynamiques classiques**
- **2 groupes: sevoflurane pour maintenir BIS entre 40 et 60**

Sufentanil administration guided by SPI versus standard practice during sevoflurane anaesthesia: a randomized controlled pilot study

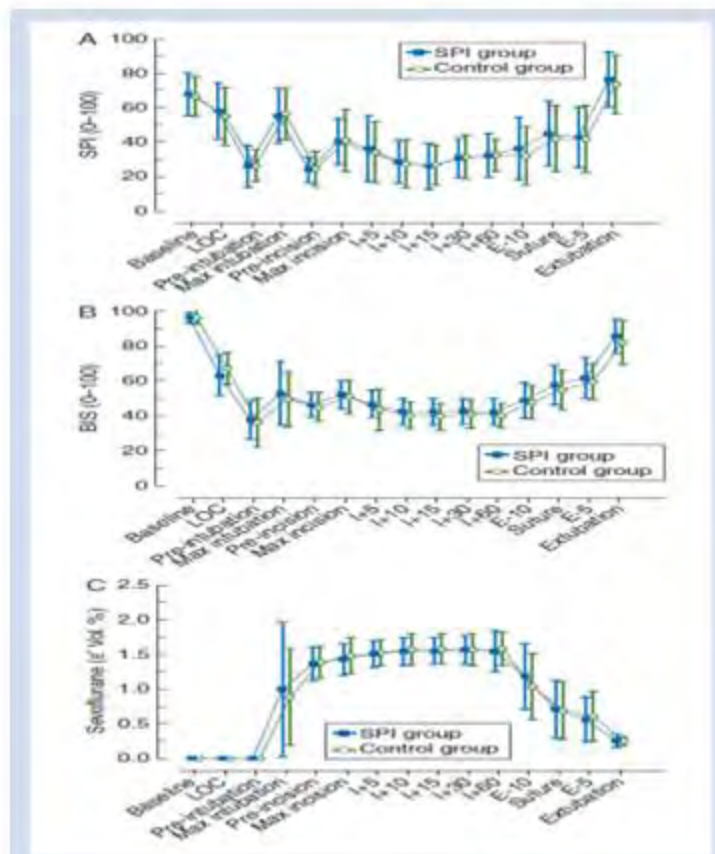
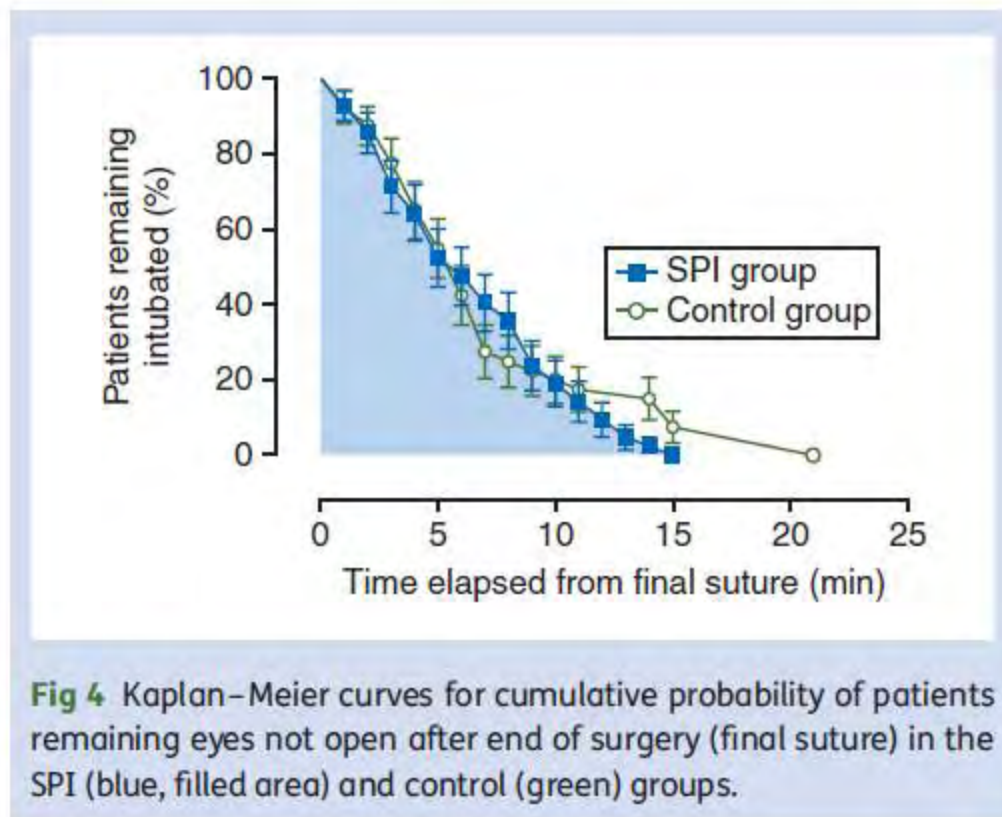


Fig 3 Characteristics for SPI (a), BIS (b), and end-tidal sevoflurane concentration (c) representing major time points during anaesthesia in the SPI (blue) and control (green) groups. Values are mean (SD). Baseline, before induction of anaesthesia; L0C, loss of consciousness; pre-intubation, before intubation; max intubation, maximum value during/after intubation; pre-incision, before start of surgery by incision; max incision, maximum value during/after incision (I); suture, final suture; E, extubation. $\pm$ values are in minutes.

Sufentanil administration guided by SPI versus standard practice during sevoflurane anaesthesia: a randomized controlled pilot study



Sufentanil administration guided by SPI versus standard practice during sevoflurane anaesthesia: a randomized controlled pilot study

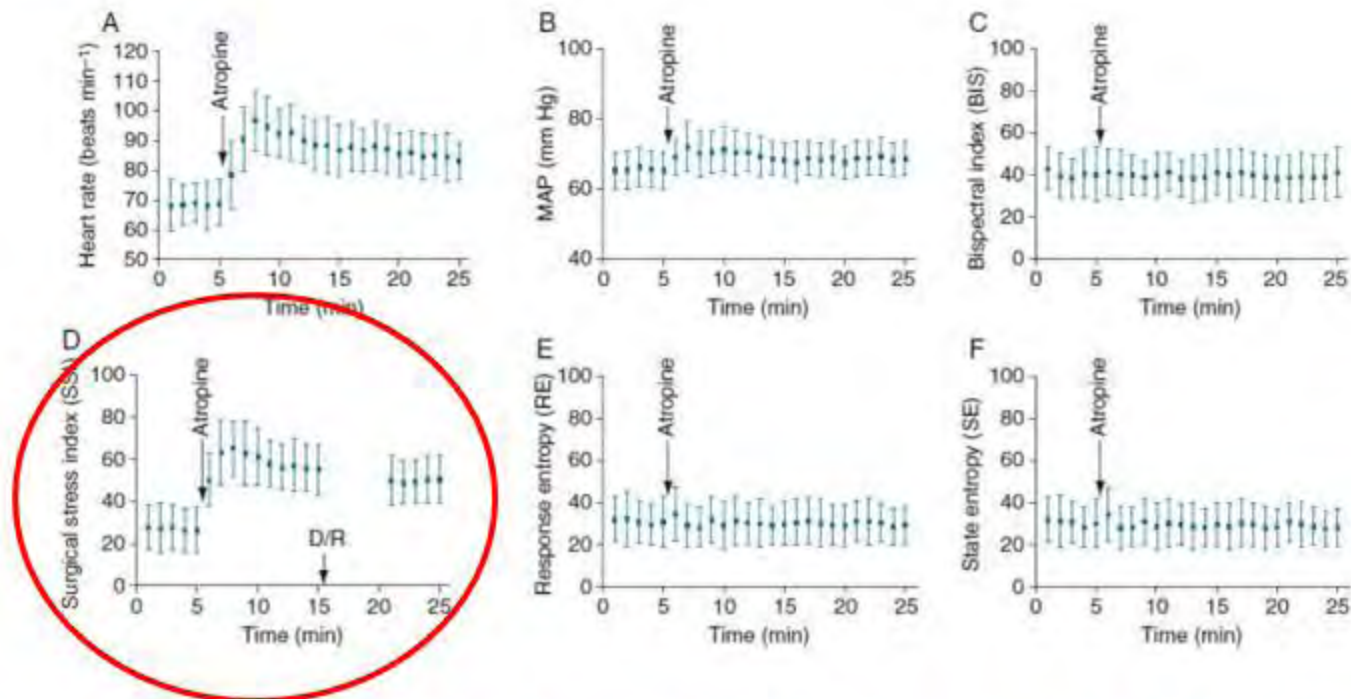
- Pas $\neq$ significative fréquence épisodes hypo ou hypertension
- Consommation moyenne SUF /minute non significativement $\neq$ groupe SPI : 0.64 (0.57–0.71) vs groupe HD : 0.78 (0.64–0.91) μg

→Hypothèse:

**technique anesthésie (remi-propofol versus sufentanil-SEVO)
influence les bénéfices de la titration remifentanil via index SPI**

$$SPI = 100 - (0.3 \times HBI_{norm} + 0.7 \times PPGAnorm)$$

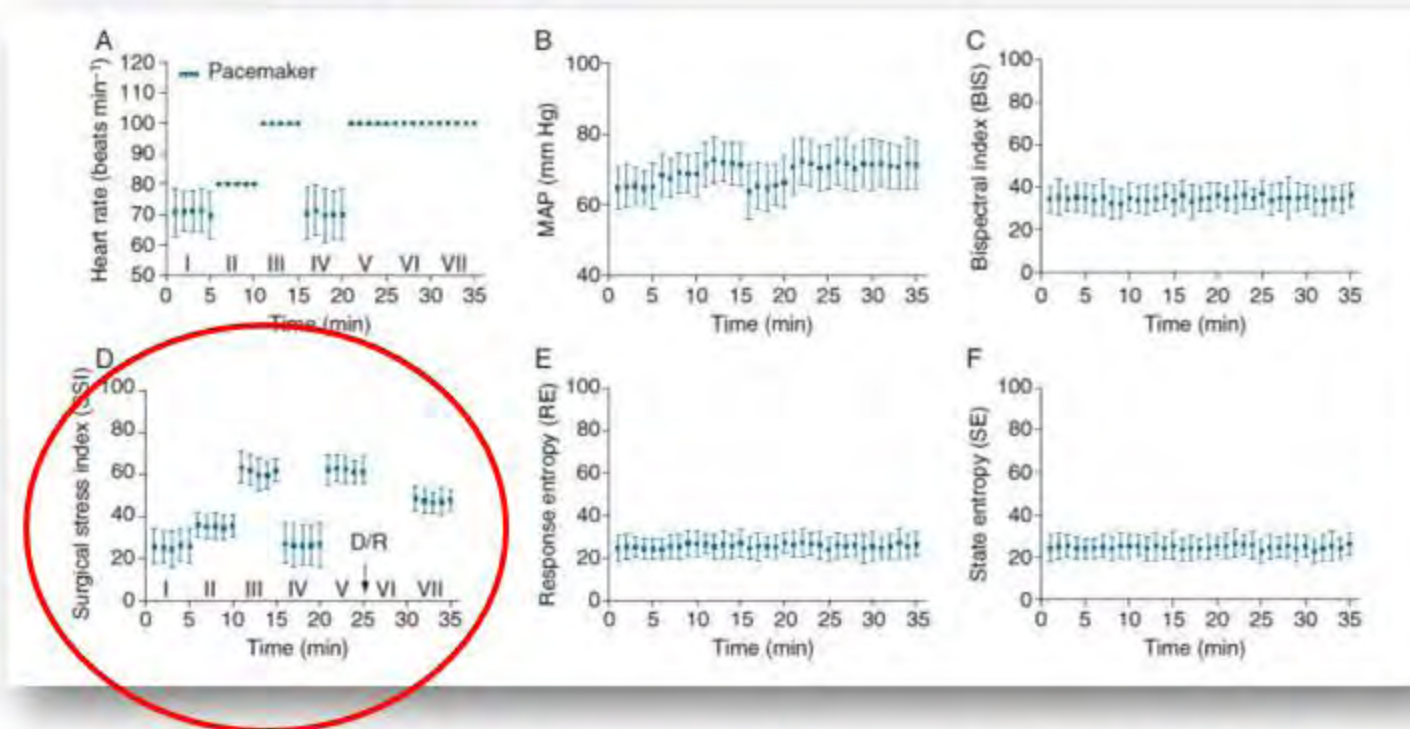
Atropine



Hocker et al., British Journal of Anaesthesia 2010; 105 (2): 150-4

$$SPI = 100 - (0.3 \times HBI_{norm} + 0.7 \times PPGAnorm)$$

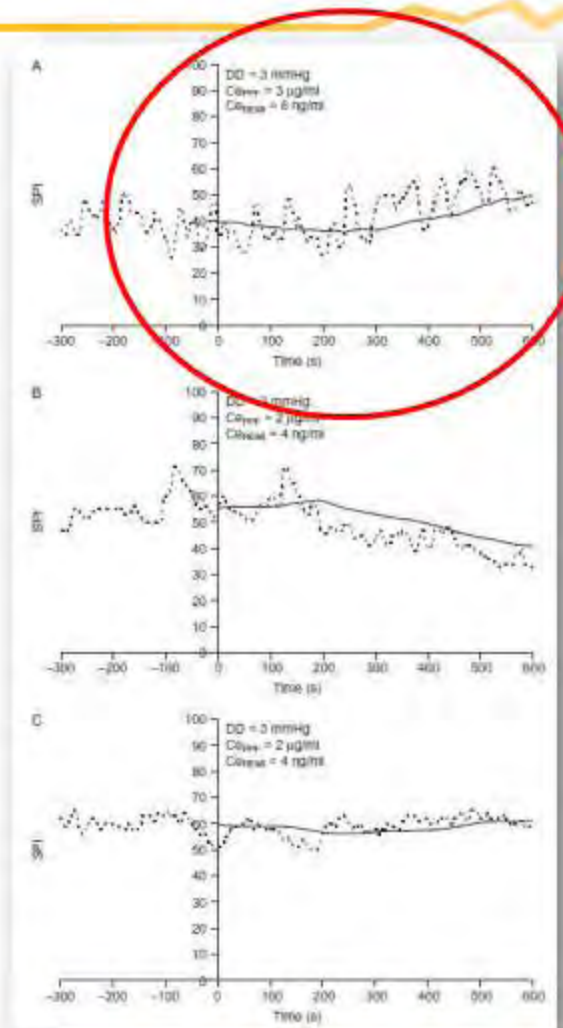
Pacing cardiaque



Effect of a fluid challenge on the SPI™ during stable propofol remifentanyl anaesthesia

- Fluid challenge
4 ml/kg starch

- N = 33



Increase N = 12

Decrease N = 3

No change N = 12

The effect of posture and anaesthetic technique on the surgical pleth index



- 45 patients randomisés : AG (n=15) ou Rachi + sédation (n=15) ou Rachi sans sédation (n=15)
 - Après adoption position lithotomie: valeurs moyennes SPI
 - ↓ 57 (22) → 21 (6) sous AG
 - ↓ 63 (15) → 31 (9) sous Rachi seul
 - ↓ 52 (14) → 22 (8) sous Rachi + sédation
- **Changement de position peropératoire influence l'index SPI pendant une durée parfois de 45 min**

Conclusions index SPI

Avantages

- Non invasif
- Complémentaire EEG
- Pas influencé par propofol
- Mesure réponse O₂ et p_e niveau analgésie Remif?

Inconvénients

- Validé uniquement patients ASA I-II
- Ne mesure pas analgésie SUF
- Influence nombreux artefacts:
 - vasoconstriction
 - hypovolémie
 - hypothermie

4 min après intubation



Quel monitoring de la balance NAN?

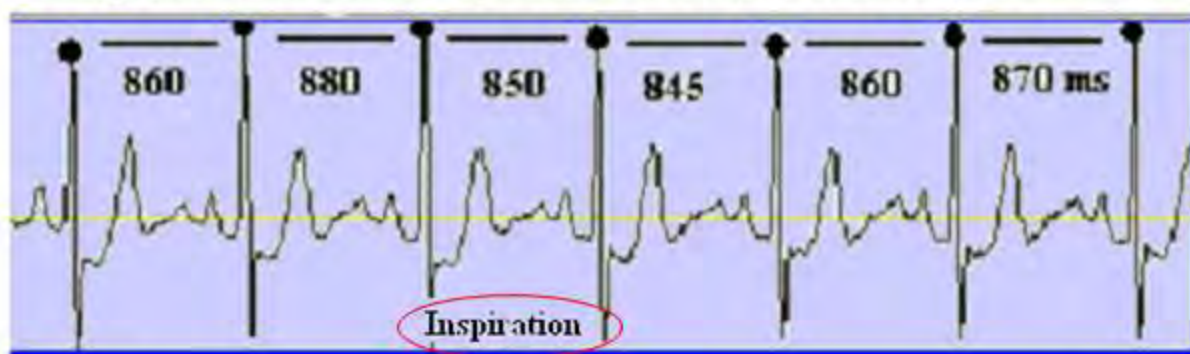


- Pression artérielle
- EEG
- SPI = Index pléthysmographique
- Variabilité du RC (AND)

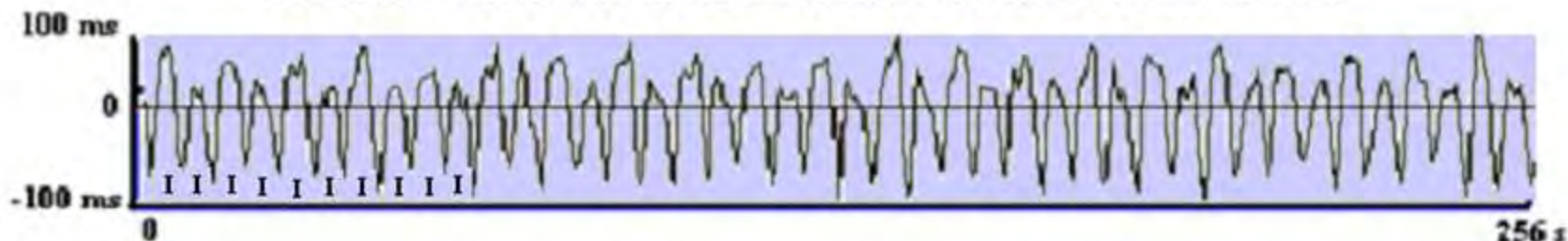
Arythmie sinusale respiratoire

Chaque cycle inspiratoire $\rightarrow$ $\downarrow$ tonus para Σ
 $\rightarrow$ $\downarrow$ intervalle RR $\rightarrow$ $\uparrow$ fréquence cardiaque

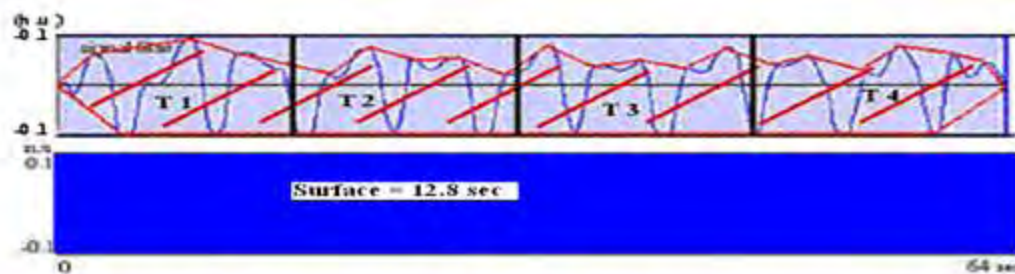
ECG, détection des ondes R, création de la série R-R unidimensionnelle



Transformation en série R-R bidimensionnelle centrée sur sa moyenne

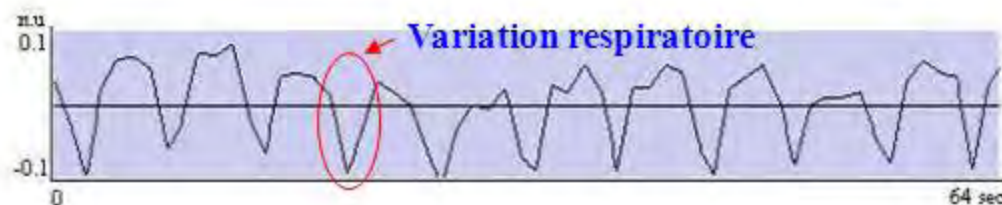


Analgesie Nociception Index (ANI)



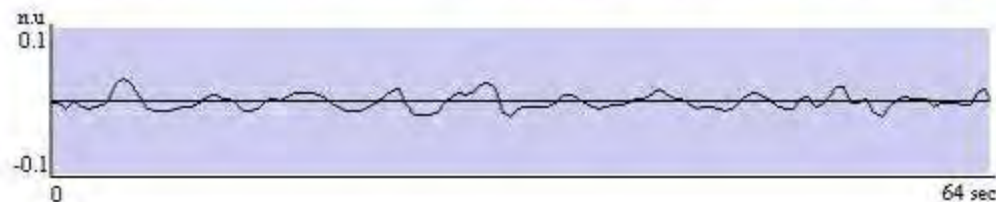
$$ANI = 100 * AUC_{tot_{nu}} / 12,8$$

Pas stimulus D⁺: seule l'arythmie sinusale respiratoire influence intervalle RR



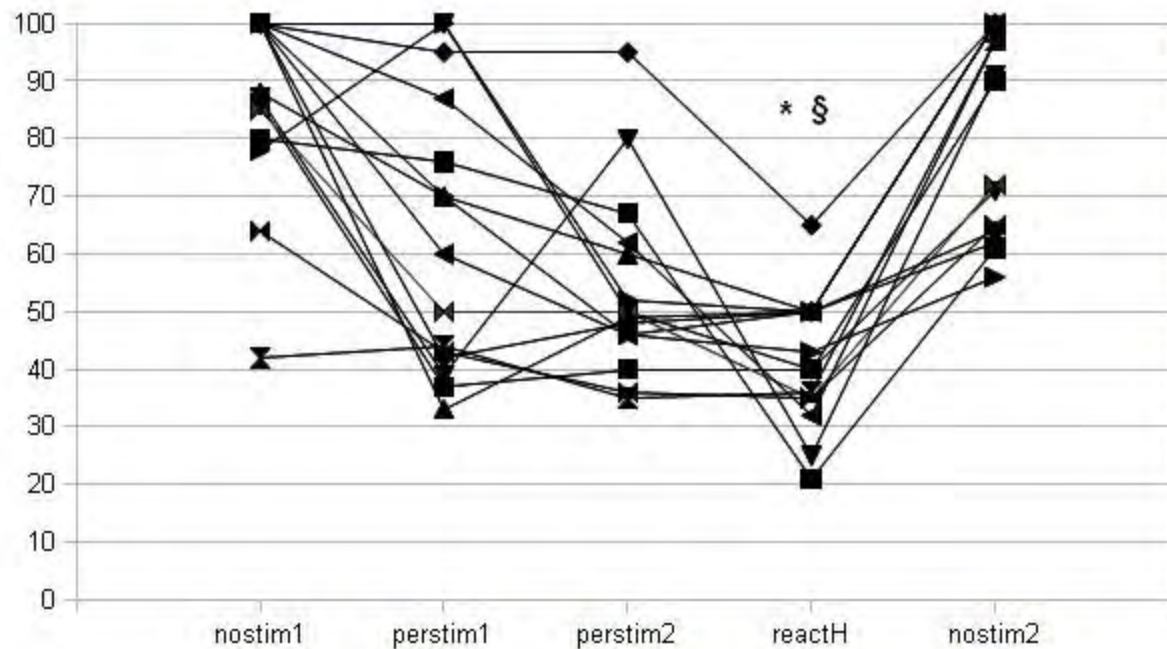
ANI > 80

Douleur, stress, anxiété: série RR devient chaotique et ↓ variation intervalle RR



ANI < 50

Variations of the Analgesia Nociception Index during general anaesthesia for laparoscopic abdominal surgery



- 15 patients adultes ASA 1/2
- Propofol : BIS [40-60]
- Remifentanyl : RC et/ou TAS $\pm 20\%$ valeurs de base
- ANI caché à l'anesthésiste
- Hémodynamique et ANI enregistrés pdt chirurgie

ANI plus sensible que variations RC et TAS aux stimuli nociceptifs

Influence of nociceptive stimulation on ANI during propofol–remifentanil anaesthesia



- **25 patients: propofol AIVOC, cible BIS: 30–60**
- **Mise en place masque laryngé → remifentanil Ce ↑ 0, 2, 4 ng/ml**
- **Chaque étape: stimulation téтанos**
- **ANI, SPI, BIS, RC et TAS mesurés avant et après insertion ML et à chaque téтанos**

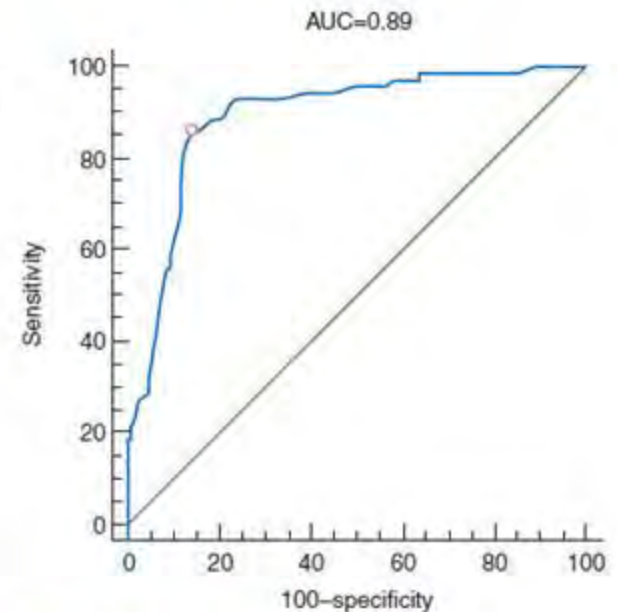
Influence of nociceptive stimulation on ANI during propofol–remifentanil anaesthesia

- ANI et SPI, mais pas BIS, RC ou TAS modifiés significativement ($P < 0.05$) à chaque stade
- Δ ANI/TET STIM = (median) -24, -30, -13 à remiCe 0, 2, 4 ng/ml
- Prédiction au mouvement à TET STIM n'était pas meilleure que la chance (valeurs PK = 0.41 ANI et 0.62 SPI)

Prediction of immediate postoperative pain using the analgesia/nociception index: a prospective observational study

E. Boselli^{1,2*}, L. Bouvet¹, G. Bégou¹, R. Dabouz¹, J. Davidson¹, J. -Y. De
and B. Allaouchiche^{1,2}

**ANI <50 avant extubation prédictif
D⁺ modérée à sévère (VAS>3)**



→ ANI pourrait aider à *anticiper* la D⁺ à la fin de chirurgie
et pourrait aider anesthésiste optimisation Θ D⁺ aiguë?

Index ANI: index HRV et tonus paraΣ



Quel monitoring de la balance NAN?



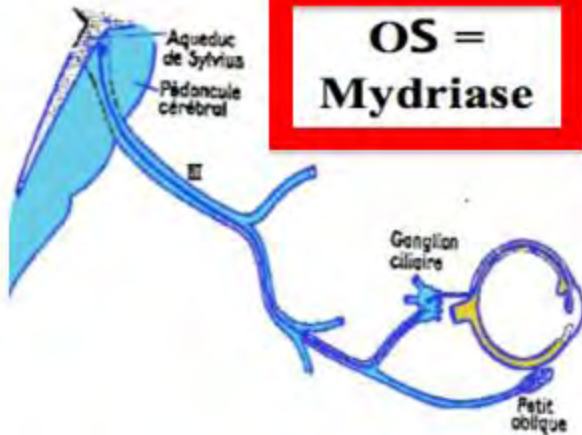
- Pression artérielle
- EEG
- SPI = Index pléthysmographique
- Variabilité du RC (AND)
- Pupillométrie

Réflexe Dilatation Pupille



**Stimulus Nociceptif
Sous AG**

**OS =
Mydriase**

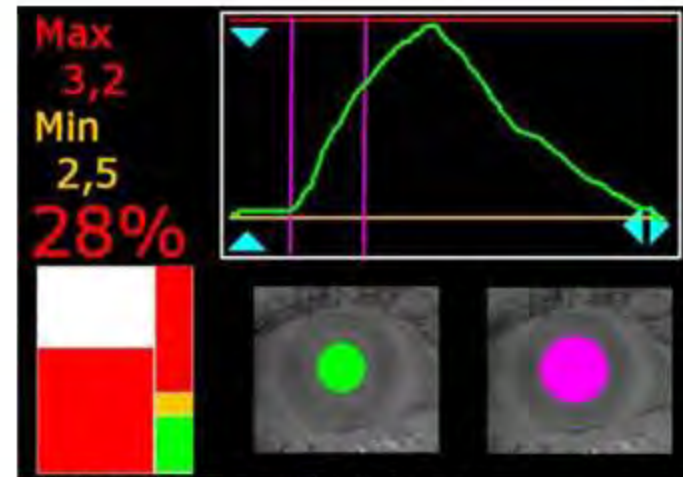


Inhibition paraΣ

**PS =
Myosis**



Réflexe Dilatation Pupille



Adapté pour l'anesthésie et USI

www.idmed.fr

Réflexe Dilatation Pupille



VidéoAlgoGraphe Synapsys*



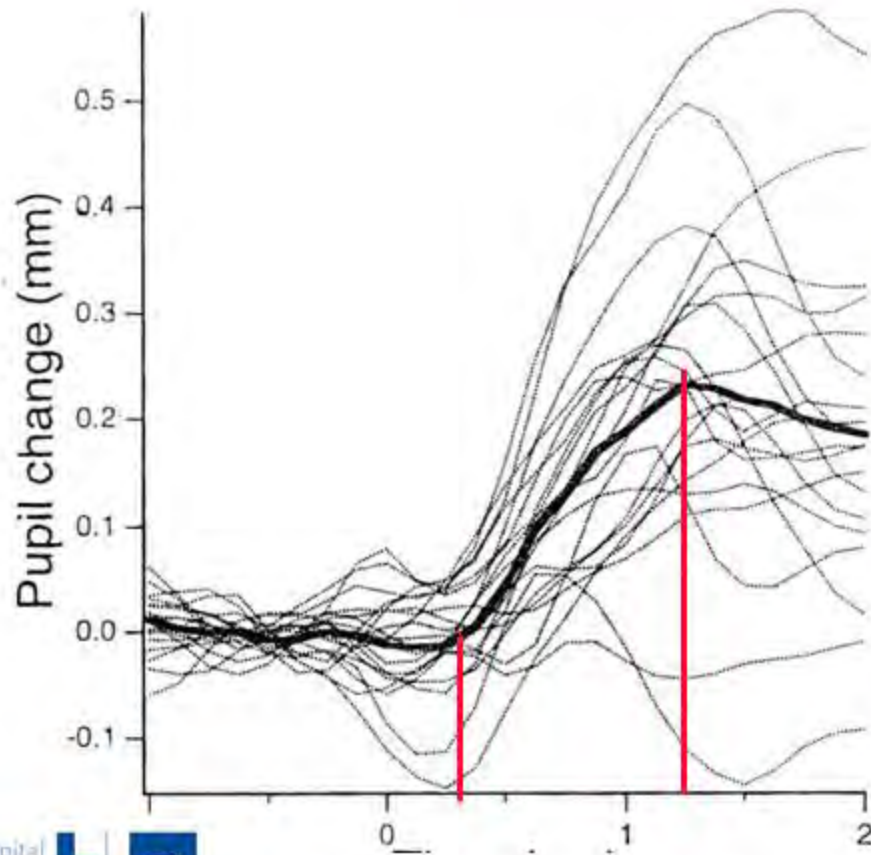
Caméra

Bis



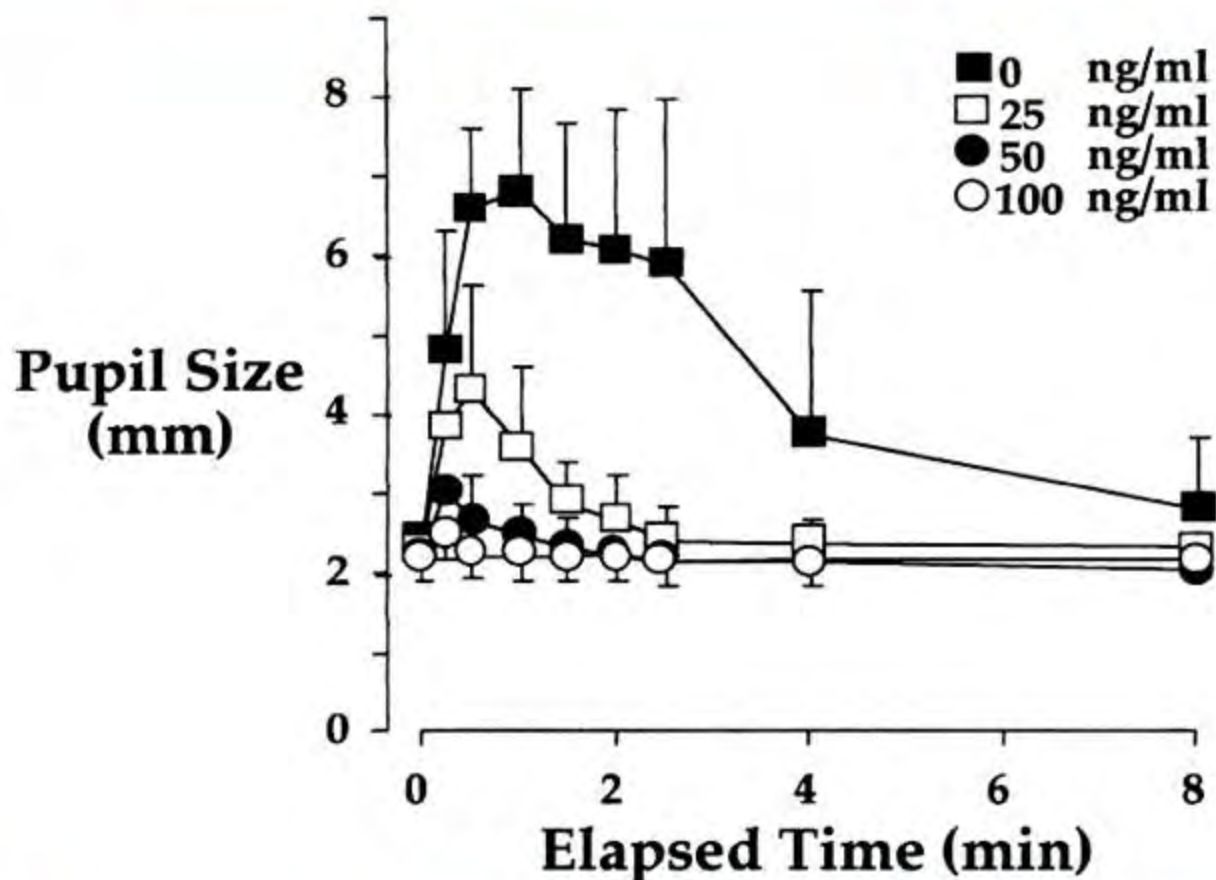
Analyse de contraste
entre l'iris et la pupille

Réflexe Dilatation Pupille



- Latence: 0.33 sec.
- PRD max: 1.25 sec.
- Pas de fatigue du RDP
- $\uparrow$ Intensité stimulation $\uparrow$ PRD
- $\text{♂} = \text{♀}$.

Alfentanil blocks reflex pupillary dilatation in response to noxious stimulation but does not diminish the light reflex



Larson M, Anesthesiology, 97 ; 87(4) : 849-55

Propofol
concentration

$\mu\text{g/ml}$

8

6

4

2

Remifentanil
concentration

ng/ml

8

7

6

5

4

3

2

1

0

10

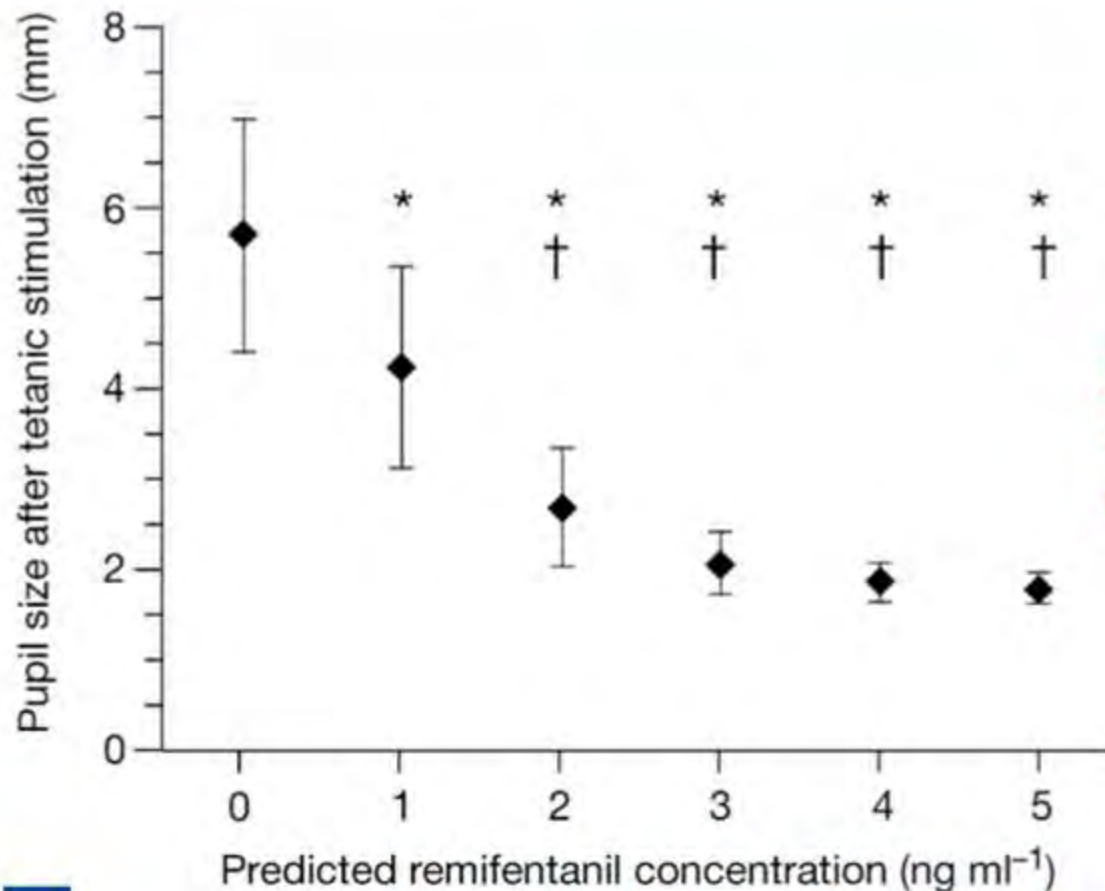
20

Time (minutes)

12 patients
Chirurgie mineure
Propofol/remifentanil AIVOC
Tetanos 100 Hz



Effect site concentrations of remifentanyl and pupil response to noxious stimulation



↓ RDP est un meilleur indice de ↑ progressive du remifentanyl Ce → 5 ng/ml que hémodynamique et BIS

Reflex pupillary dilatation in response to skin incision and alfentanil in children anaesthetized with sevoflurane

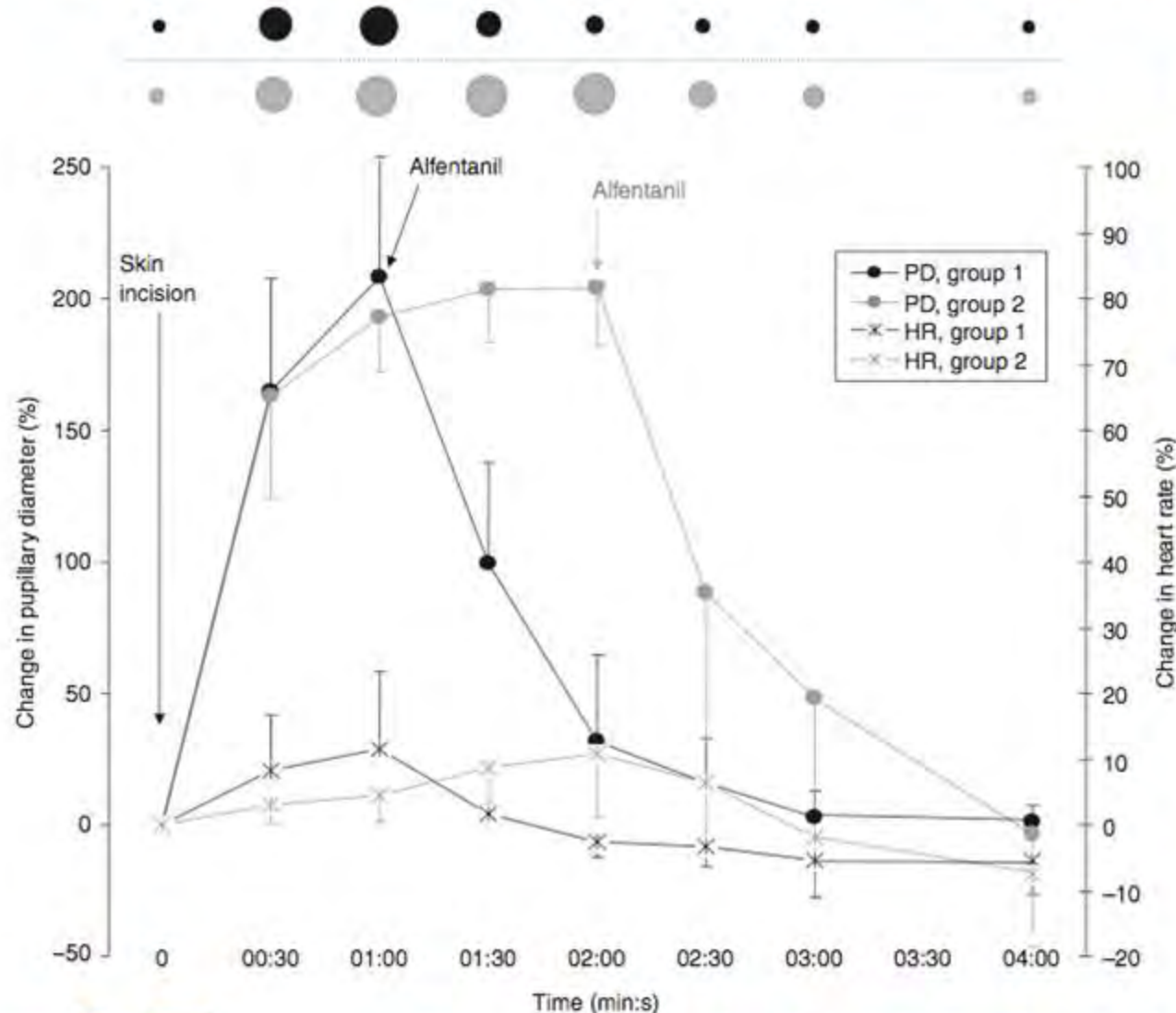
24 enfants

Sevorane 1,5 MAC

Incision cutanée

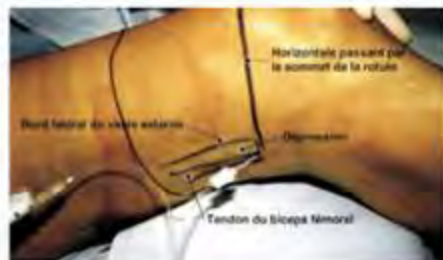
alfentanil 10 mcg/kg
après 1 ou 2 min

**RDP est un meilleur
indice de la stimulation
nociceptive que BIS ou
RC et TAS chez enfant**



Pupillometry to detect pain response during general anaesthesia following unilateral popliteal sciatic nerve block: a prospective, observational study

- 24 patients adultes programmés pour chirurgie pied ou cheville sous AG
- RDP à la stimulation tetanos différente selon la jambe avec ou sans bloc



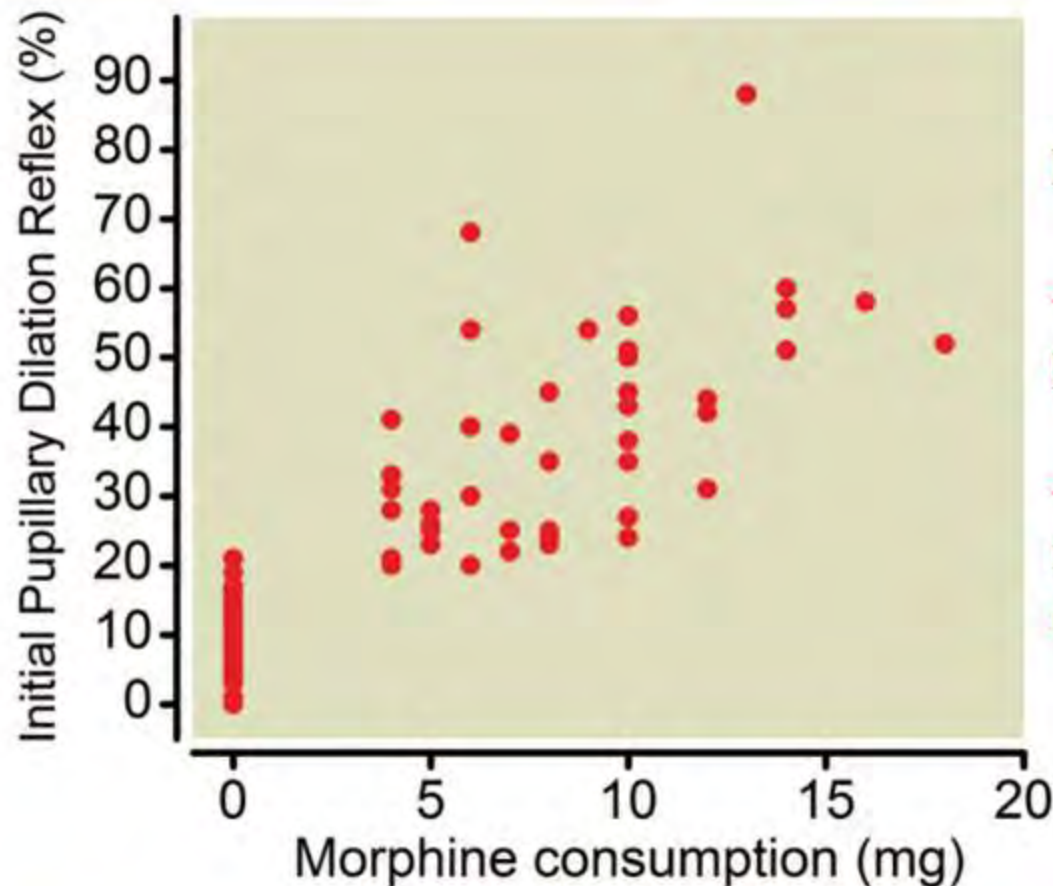
AG

RDP côté bloqué ?
2%

RDP côté non bloqué ?
17%



Objective assessment of the immediate postoperative analgesia using pupillary reflex measurement. A prospective study



PRD = méthode objective

- pour évaluer analgésie postopératoire

- pour aider la titration de morphine, spécialement chez patients débilisés

Conclusions RDP

Avantages

- Non invasif
- Pas usage unique
- Bon monitoring ALR sous AG
- Mesure niveau analgésie opiacé
- Prédiction D⁺ postop?

Inconvénients

- Monitoring non continu
- Nécessite Tétanos ou stimulus NOCI



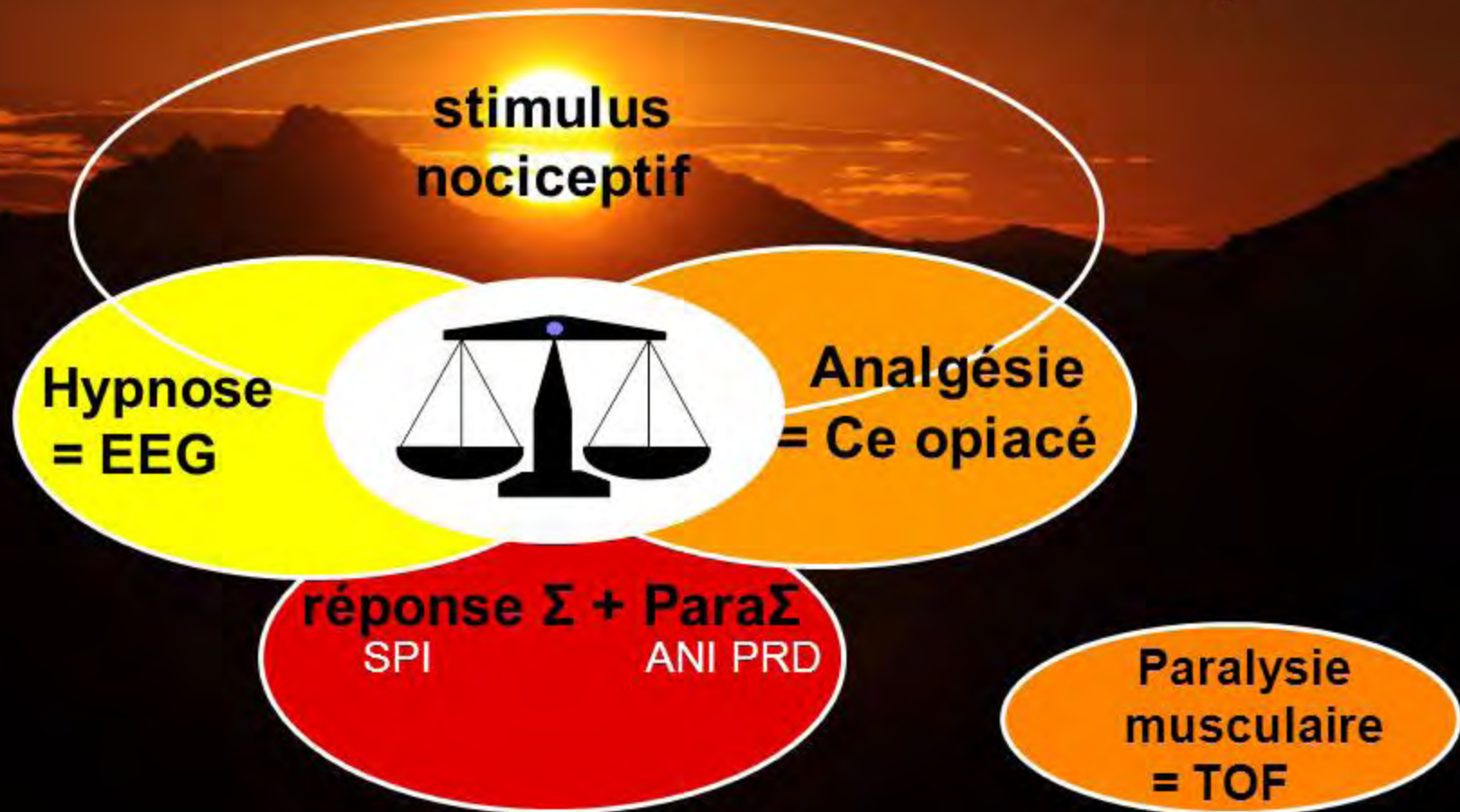
Quel monitoring choisir?

Anesthésiste essaie développer monito idéal balance NAN

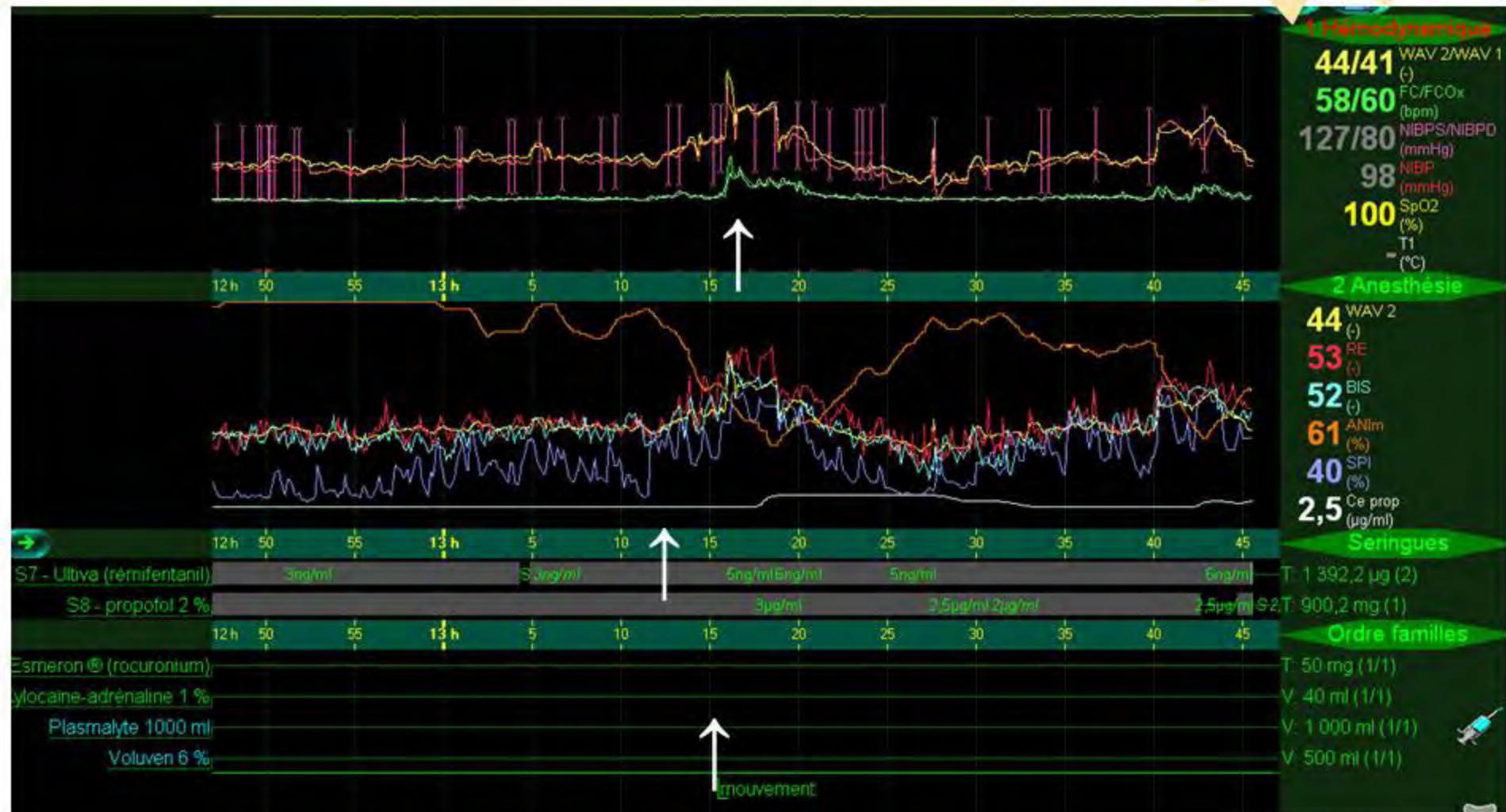
- ↑ si intensité stimulus nociceptif ↑
- ↓ si analgésie ↑

- Depuis 10 ans: ≠ nouveaux index: SPI, ANI, RDP mais aucun parfait pour mesurer analgésie multimodale!

Quel monitoring choisir?



Episode mouvement





Combinaison des $\neq$ techniques?

Couplé avec intensité stimulus et Ce opiacé?

Monitoring the nociception level: a multi-parameter approach

Nir Ben-Israel · Mark Kliger · Galit Zuckerman ·
Yeshayahu Katz · Ruth Edry

- **25 patients (propofol remifentanyl + sevo pour entretien)**
- **Variabilité RC (0.15–0.4 Hz band power), amplitude onde pléthysmographie conductance cutanée, incorporés dans un seul index (NoL)**
- **NoL index permet de mieux discriminer les événements chirurgicaux noci et non nociceptifs comparés aux paramètres individuels**
- **Nécessité de validation dans ≠ populations**
 - ≠ types d'anesthésie
 - ≠ stimuli nociceptifs

Comparison of the Surgical Pleth Index™ with haemodynamic variables to assess nociception-anti-nociception balance during general anaesthesia

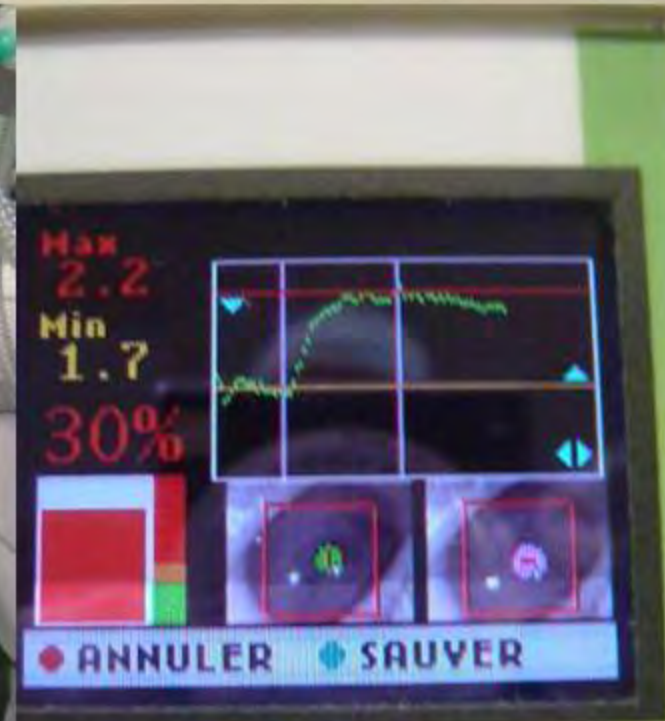
Table 4. Prediction accuracy of ordinal regression models. APR, accurate prediction rate; Pk, prediction probability calculated using actual remifentanyl concentration against predicted concentration by (1) DO, (2) DO and MAP, (3) DO and HAP. 95% CI, confidence interval (95% CI). Abbreviations of independent variables are identical to those in Table 3. Those parameters are given for the models described in the Methods section and for the situation where models #3 for SPI, HR, and MAP are concordant in their prediction. n corresponds to the number of patients where concordance occurred. *PK's that are significantly different from 0.5

Independent variables	Model #	Additional independent variables	APR	Pk (n), 95% CI
SPI	1	None	0.50	0.63 (0.089), 0.44–0.81
	2	DO	0.57	0.70* (0.084), 0.53–0.87
	3	DO and HAP	0.60	0.76* (0.072), 0.61–0.90
HR	1	None	0.57	0.74* (0.073), 0.60–0.89
	2	DO	0.5	0.75* (0.061), 0.63–0.88
	3	DO and HAP	0.60	0.79* (0.059), 0.67–0.91
MAP	1	None	0.57	0.78* (0.065), 0.64–0.91
	2	DO	0.60	0.78* (0.067), 0.64–0.91
	3	DO and HAP	0.60	0.78 (0.067), 0.64–0.91
If models #3 are concordant in their prediction (n)				
SPI and HR (21)			0.71	0.87* (0.054), 0.76–0.98
SPI and MAP (17)			0.76	0.90* (0.049), 0.80–1.00
HR and MAP (20)			0.70	0.87* (0.045), 0.70–0.97

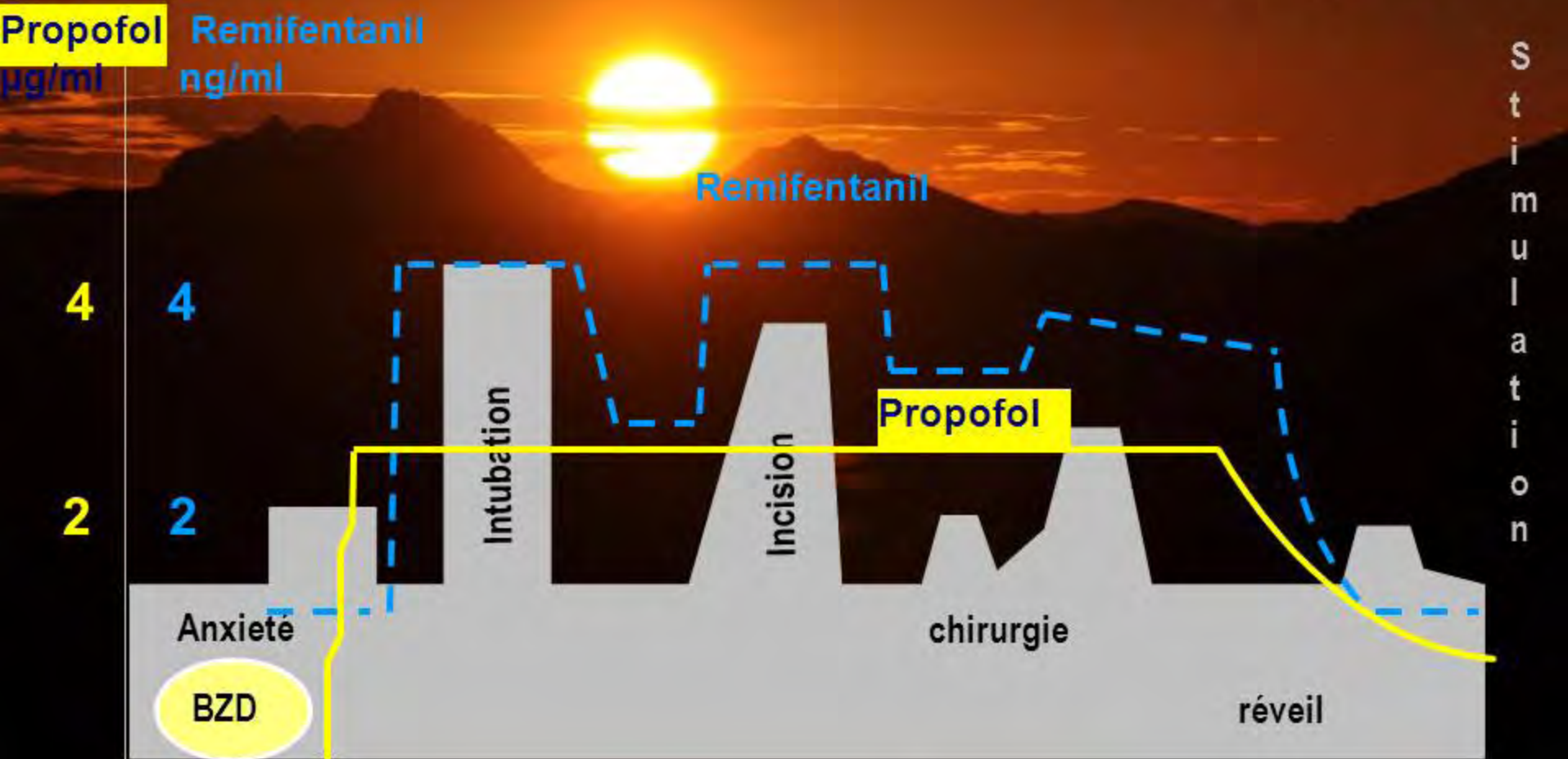
- 33 patients neurochirurgie.
- Stimulus standard = insertion tête picots
- Ce REMI (2, 4, 6 ng/ml)
- propofol cible: 3 µg/ml.

Meilleure prédiction si combinaison:

**RC
+ TAM
+ SPI
+ Status volémie
+ patient hypertensif ou pas**



En pratique clinique



Calibration: NAN ?

