

*CLUD TOULOUSE*  
*25 octobre 2007*

# **Pourquoi traiter vite et bien une douleur aiguë ?**

## **Comment ?**

*Dr Ph. Richebé*

**Le 25 octobre 2007**

**9h00 – 9h45**

## Avancées récentes considérables dans la gestion de la DPO :

- PCA
- Techniques Epidurales
- Amélioration dans la formation du personnel médical et paramédical
- Développement de centre de la douleur aiguë postopératoire
- Nouveaux agents et stratégies analgésiques / antihyperalgésiques...

**MAIS....**

# *La douleur aiguë après chirurgie persiste!!!....*

- *Dolin et al, BJA 2002*

Plus de 20000 patients : 41% ressentent encore une douleur aiguë postopératoire caractérisée comme modérée à sévère ; 24% relatent une analgésie inefficace!

- *Apfelbaum JL et al, Anesth Analg 2003*

LA DPO est toujours sous-estimée en postopératoire! (Etude nationale USA)

## **Postoperative Pain Experience: Results from a National Survey Suggest Postoperative Pain Continues to Be Undermanaged**

Jeffrey L. Apfelbaum, MD\*, Connie Chen, PharmD†, Shilpa S. Mehta, PharmD†, and Tong J. Gan, MD‡

\*Department of Anesthesia and Critical Care, The University Chicago Hospitals, Chicago, Illinois; †Pharmacia Corp., Skokie, Illinois; and ‡Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina

**Pourquoi traiter vite et bien  
une douleur aiguë ?**

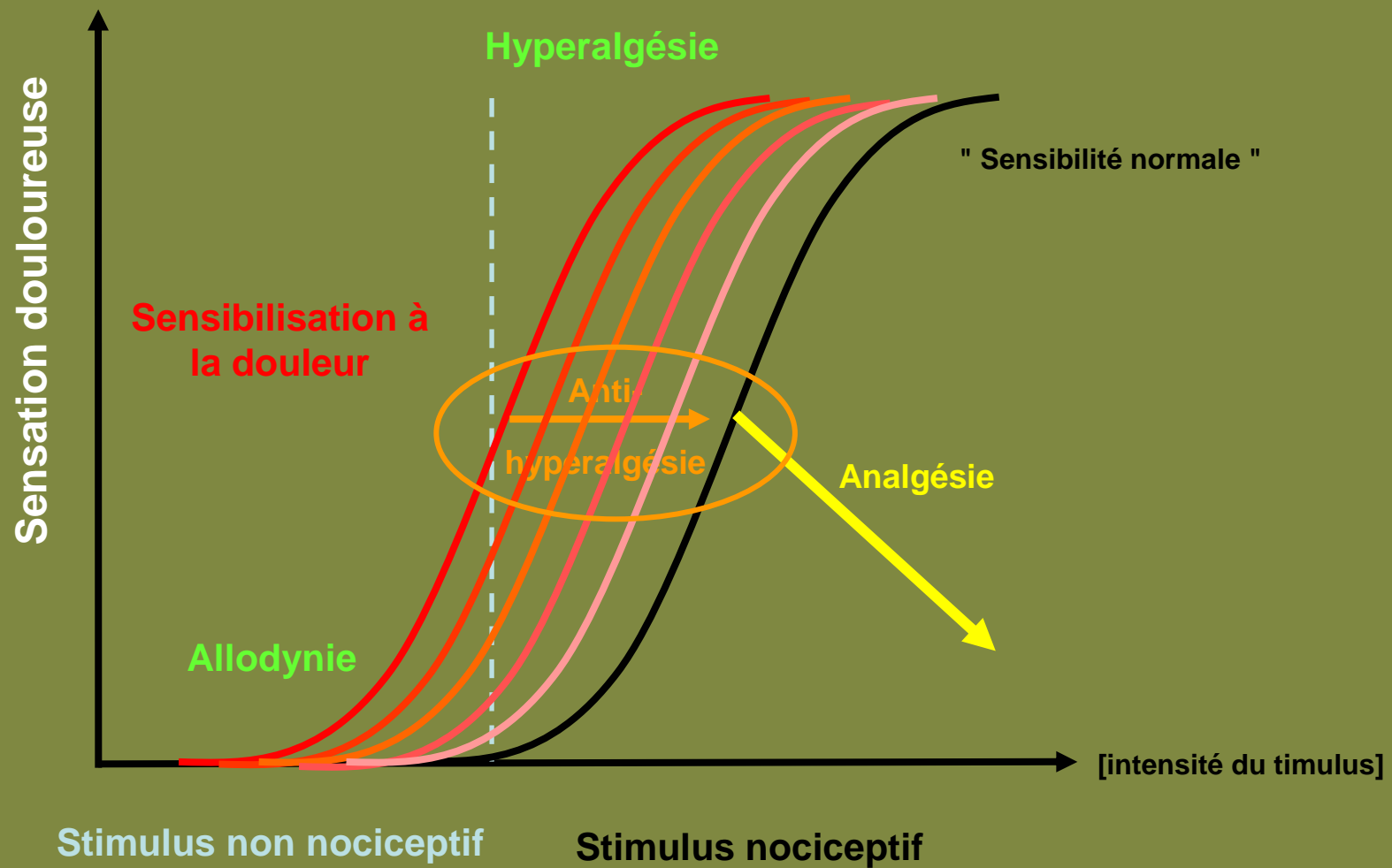
***Conséquences DPO***

**=**

***Sensibilisation***

***et***

***« HYPERALGESIES  
POSTOPERATOIRES »***



# On doit EVALUER!

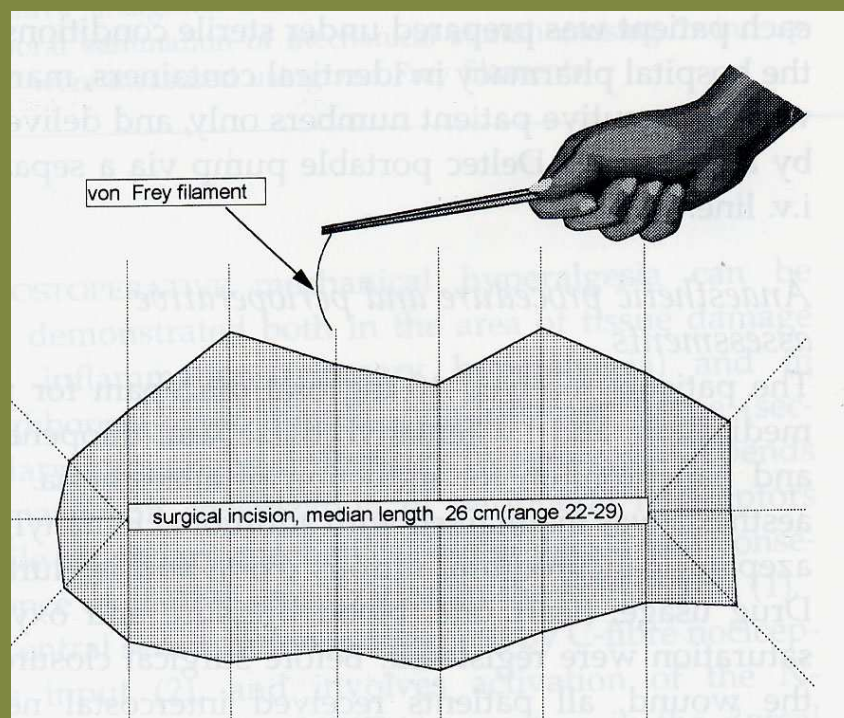


# Et quand on évalue, on trouve!

Acta Anaesthesiol Scand. 1997 Oct;41(9):1124-32.

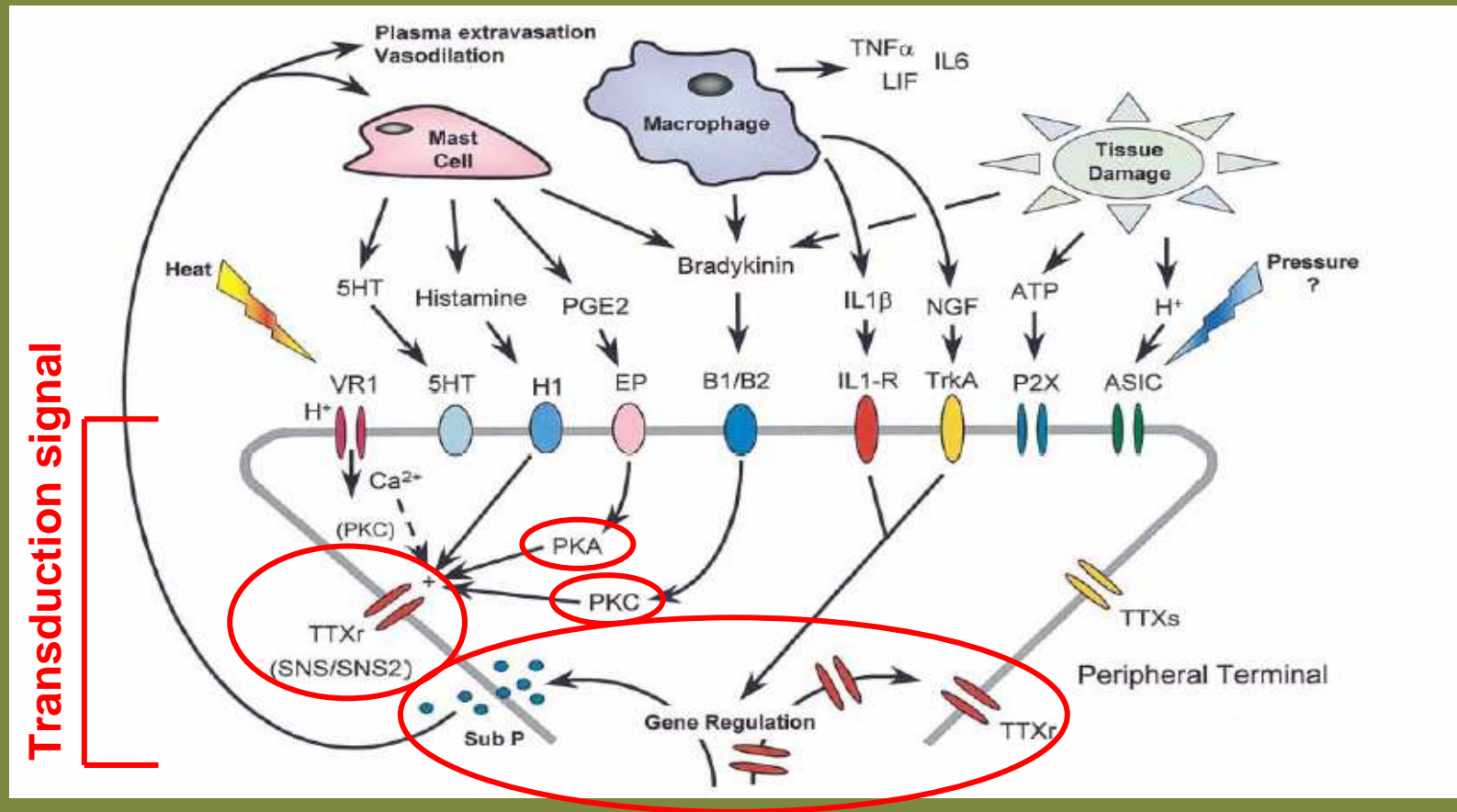
**Mapping of punctuate hyperalgesia around a surgical incision demonstrates that ketamine is a powerful suppressor of central sensitization to pain following surgery.**

Stubhaug A, Breivik H, Eide PK, Kreunen M, Foss A.

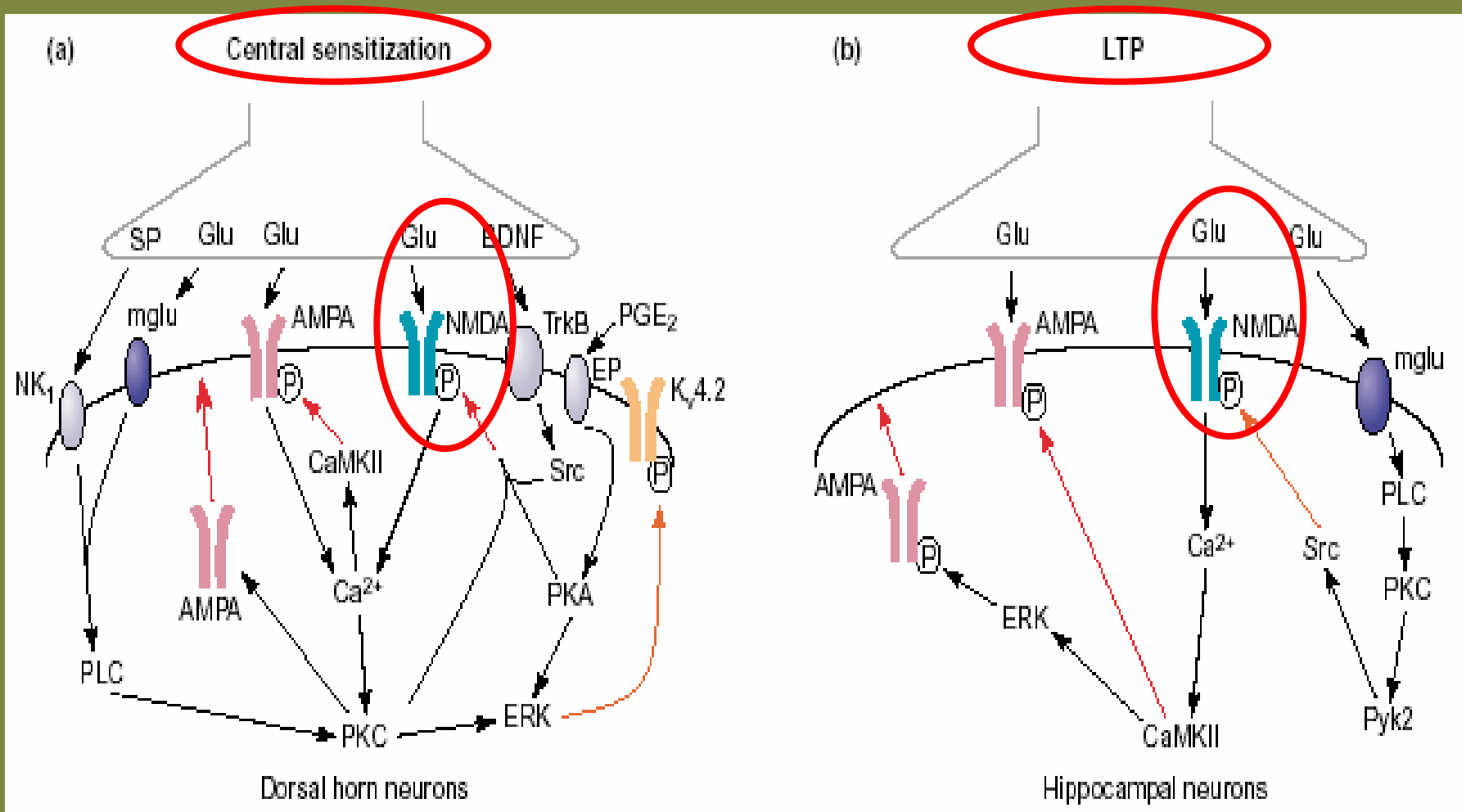




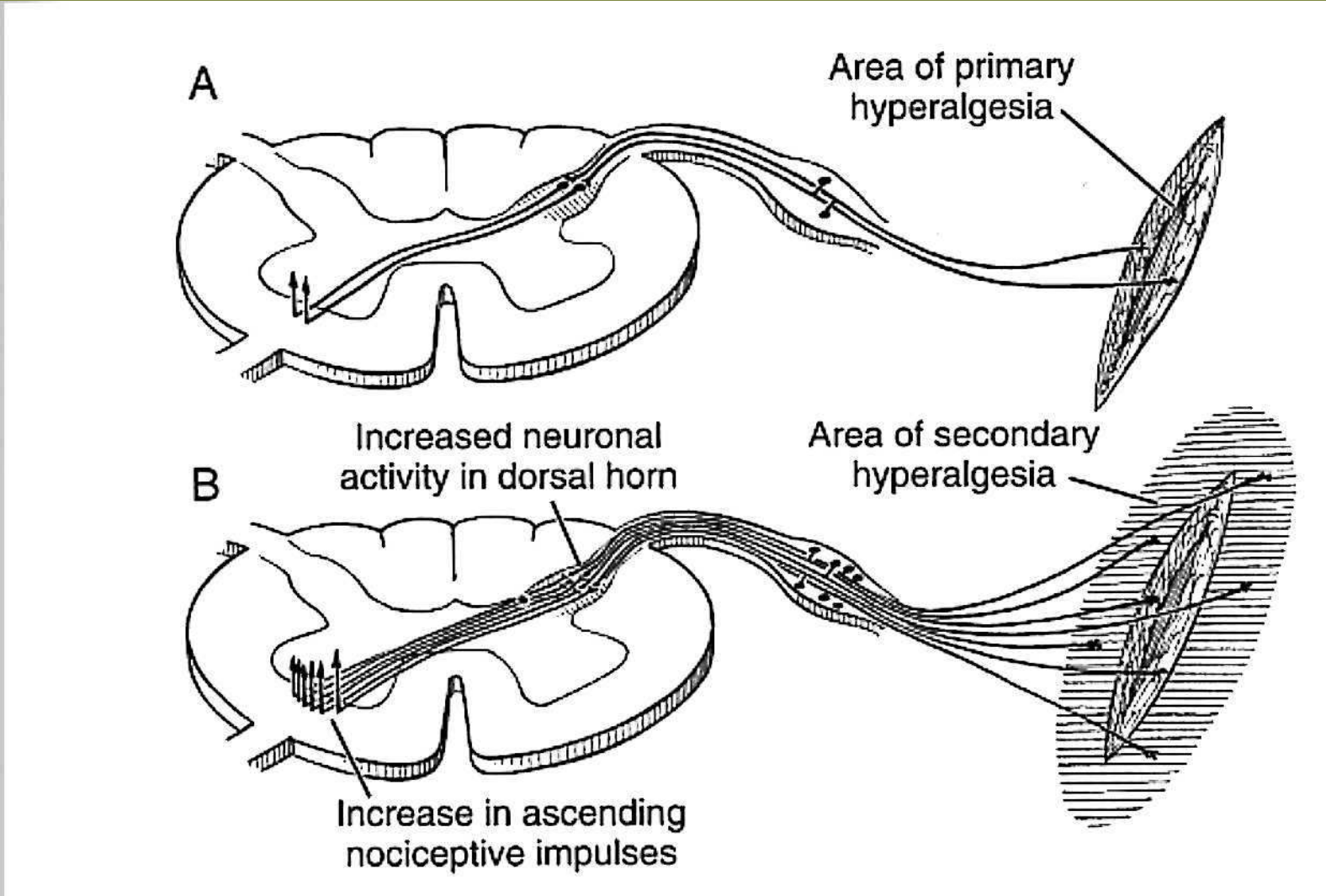
# Les bases neurophysiologiques



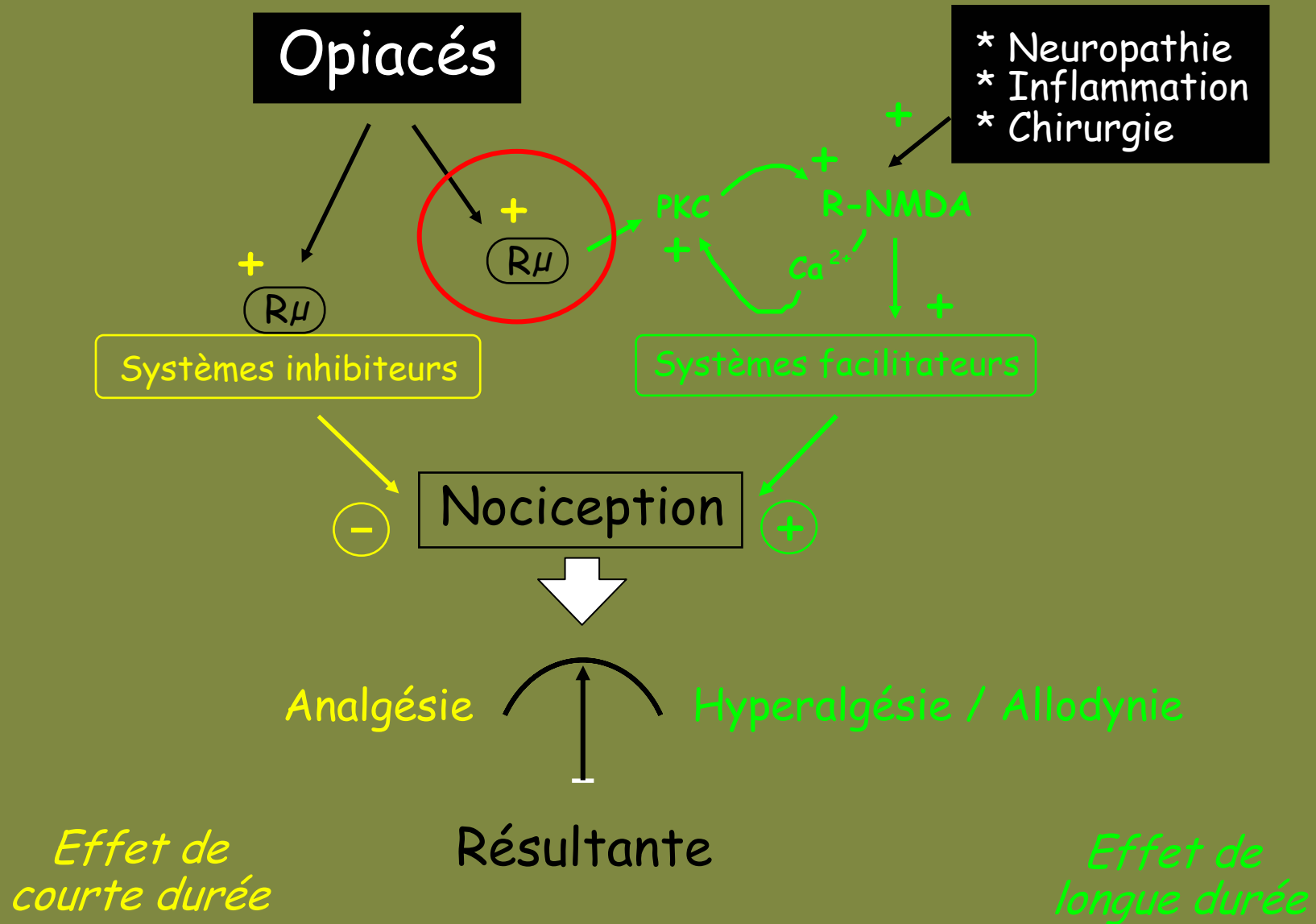
Costigan M. and Woolf C.J. *The Journal of Pain*, 2000



# Hyperalgésie Primaire et Secondaire



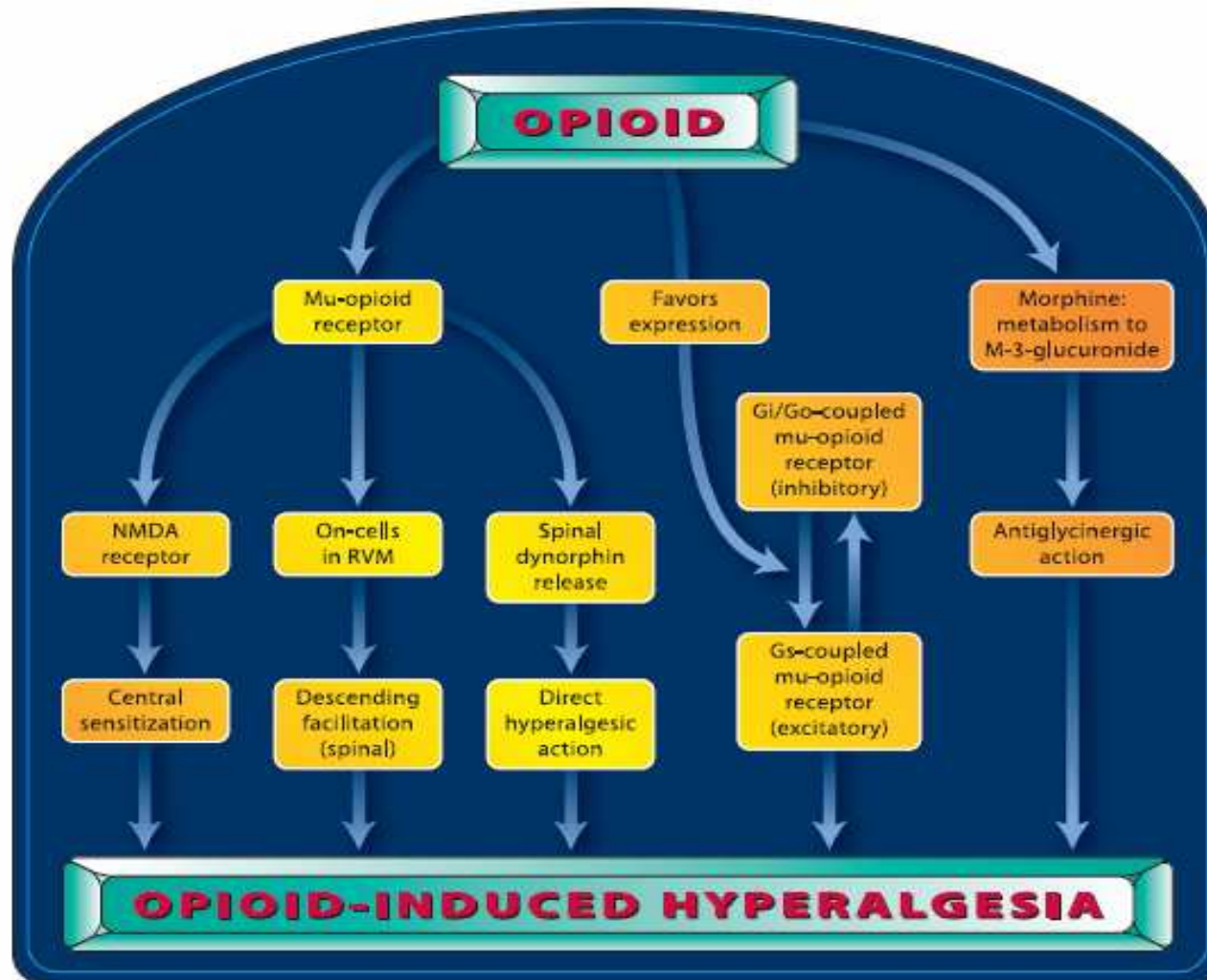
# Influence des opiacés

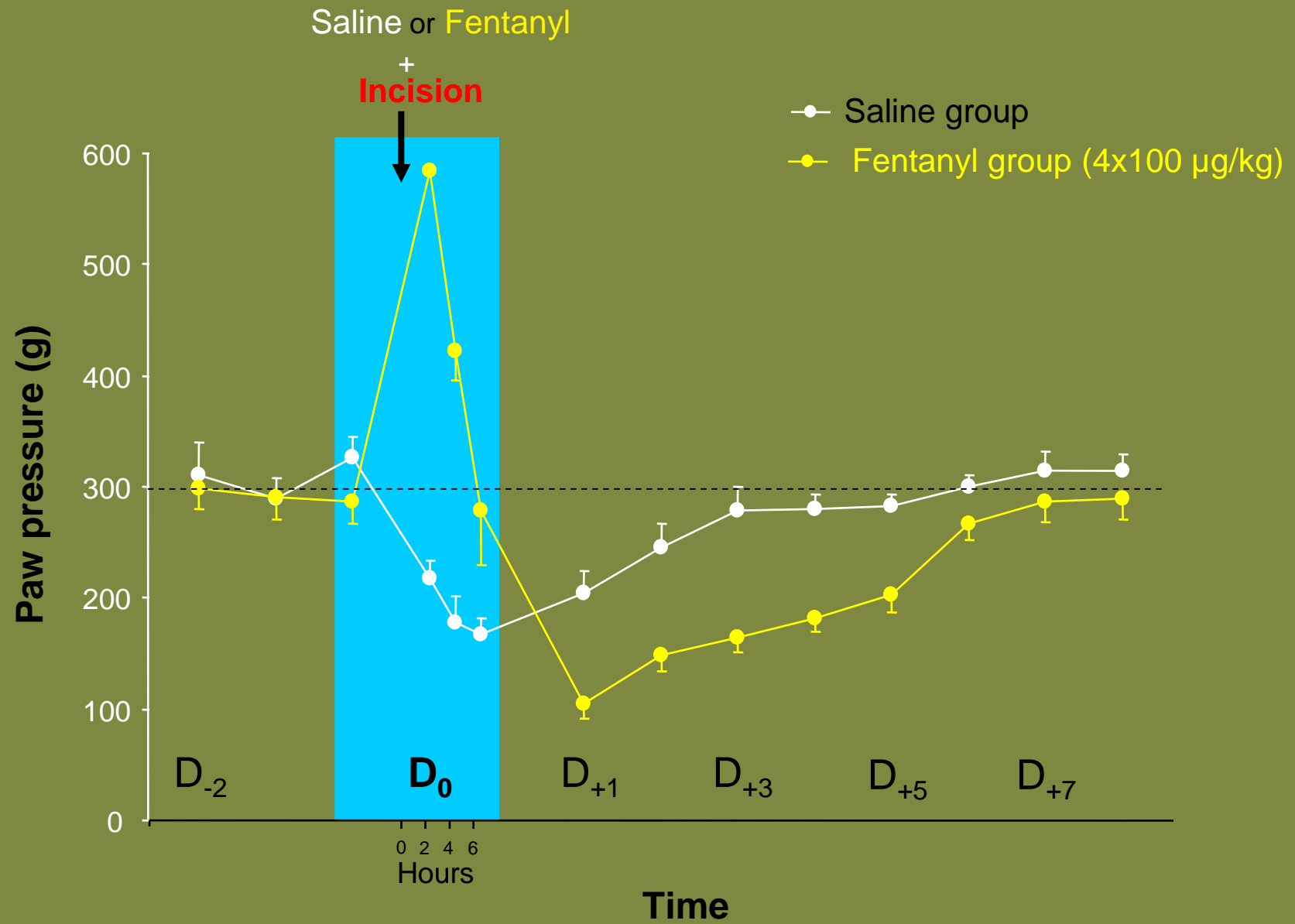


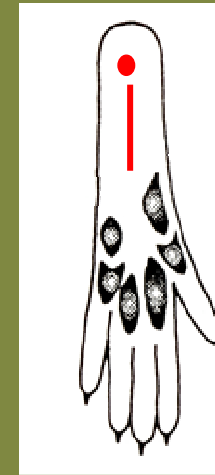
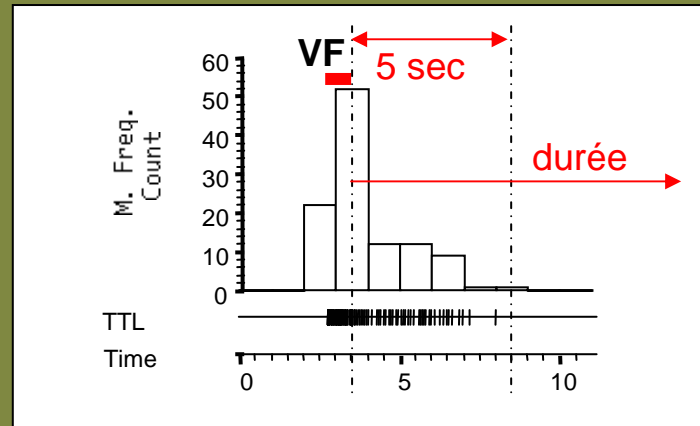
# Postoperative Hyperalgesia

## Its Clinical Importance and Relevance

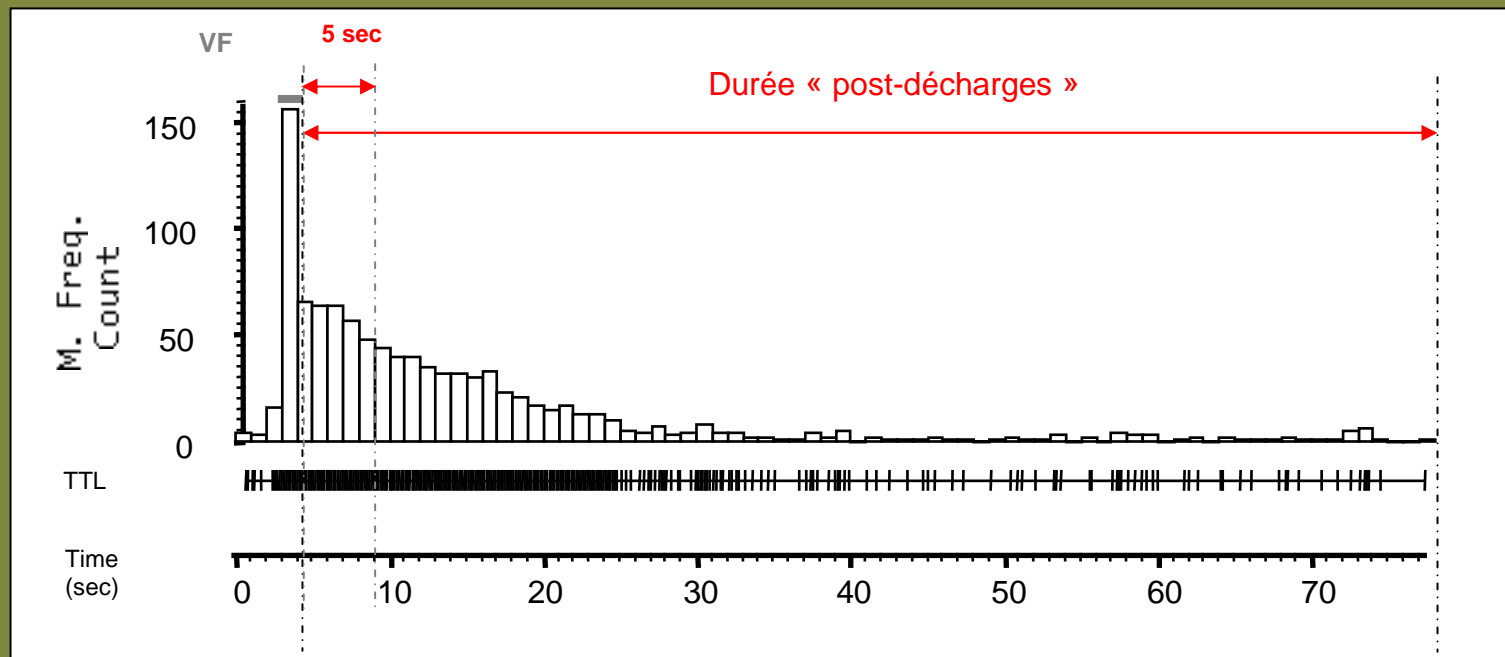
Oliver H. G. Wilder-Smith, M.B.Ch.B., M.D., Ph.D.,\* Lars Arendt-Nielsen, Ph.D., D.MSc.†



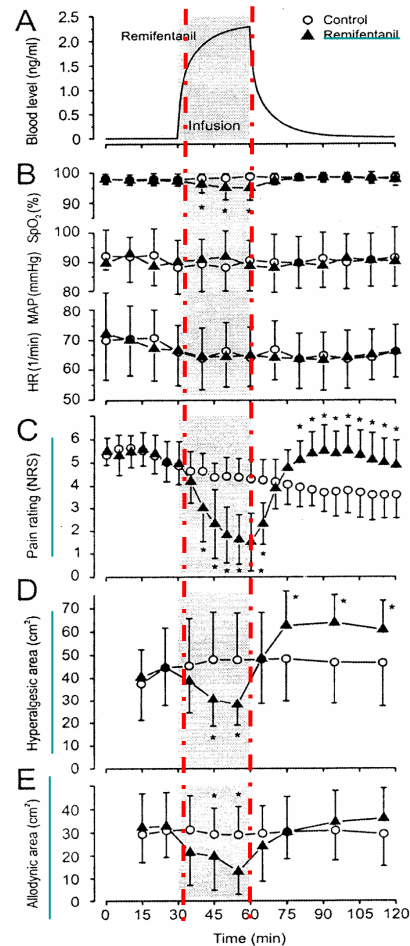




Incision seule



Incision + fentanyl



**Fig. 2.** Time course of calculated remifentanyl plasma concentrations after a constant-rate infusion of  $0.1 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  (shaded area). The calculation was based on a data sheet from the literature<sup>57</sup> exemplary for a 75-kg subject (A). Infusion of remifentanyl resulted in a significant decrease in oxygen saturation measured by pulse oximetry (SpO<sub>2</sub>) ( $P < 0.001$  by ANOVA), whereas mean arterial pressure (MAP) and heart rate (HR) remained unchanged ( $P = \text{NS}$  by ANOVA) (B). Pain ratings (C) and areas of punctate hyperalgesia (D) and touch-evoked allodynia (E) were reduced significantly during infusion of remifentanyl ( $P < 0.05$  by ANOVA for each). However, shortly after cessation of the infusion, pain ratings and hyperalgesic areas increased and exceeded control values ( $P < 0.01$  by ANOVA for each). Data are expressed as mean  $\pm$  SD ( $n = 13$ ), \* $P < 0.05$ , planned comparisons corrected with the Bonferroni procedure. NRS = numerical rating scale.



Chia Yuan-Yi et al,

Can J Anaesth 1999 / 46: 9 / 872-7

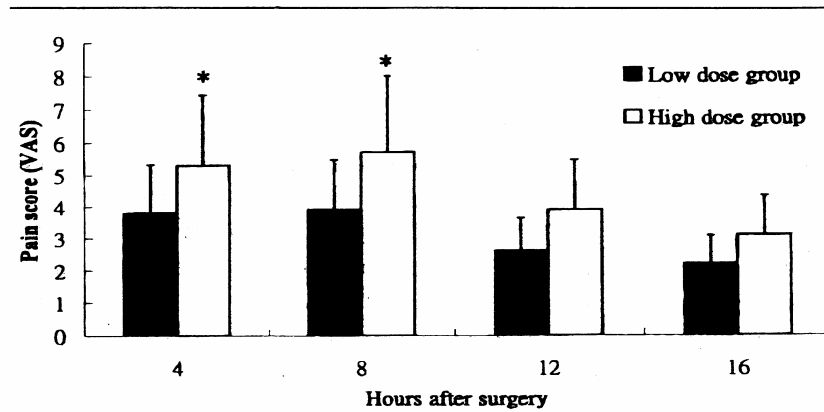


FIGURE 1 Postoperative visual analogue scores (VAS) (mean  $\pm$  SD) during the first postoperative 16 hr. \*:  $P < 0.05$ .

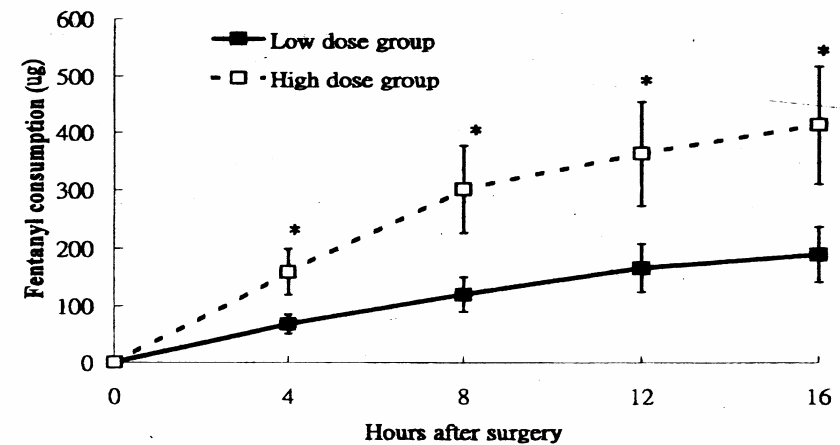
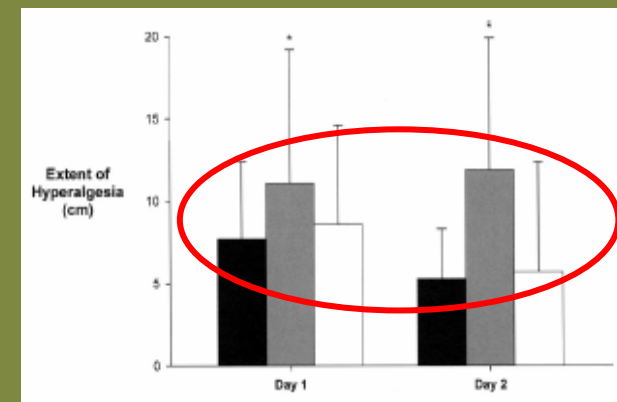
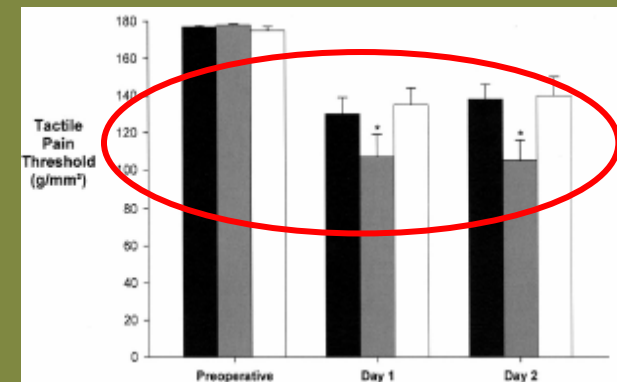
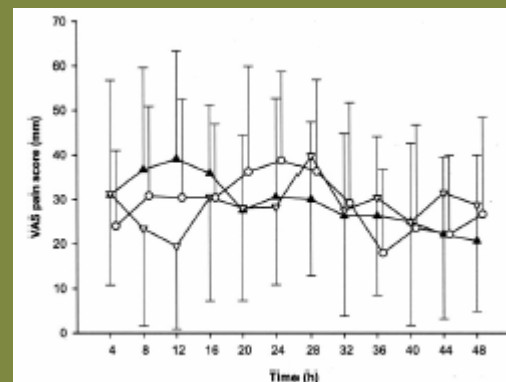


FIGURE 2 Postoperative accumulated fentanyl consumption ( $\mu\text{g}$ ) (mean  $\pm$  SD) during the first 16 hours after surgery. \*:  $P < 0.05$ .

# Remifentanyl-induced Postoperative Hyperalgesia and Its Prevention with Small-dose Ketamine

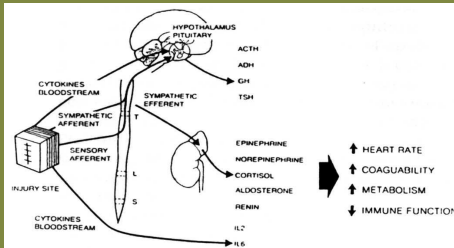
Vincent Joly, M.D.,\* Philippe Richebe, M.D.,† Bruno Guignard, M.D.,\* Dominique Fletcher, M.D.,‡ Pierre Maurette, M.D.,§ Daniel I. Sessler, M.D.,|| Marcel Chauvin, M.D.#

	Small-dose Remifentanyl (n = 25)	Large-dose Remifentanyl (n = 25)	Large-dose Remifentanyl-Ketamine (n = 24)
Remifentanyl dose, mg	0.9 ± 0.3*	6.7 ± 3.1	6.5 ± 3.4
Desflurane, MAC/h	0.8 ± 0.2*	0.5 ± 0.2	0.6 ± 0.2
Ephedrine, No. of doses/No. of patients	9/17	10/13	50/15†
Final intraoperative temperature, °C	36.6 ± 0.7	36.3 ± 0.8	36.3 ± 0.9
Awakening time, min	14 ± 6	13 ± 5	14 ± 6
Extubation time, min	16 ± 6	14 ± 6	15 ± 4
Time to first postoperative morphine, min	35 (28-46)	24 (20-33)	41 (32-52)
Morphine given in PACU, mg	16 (10-24)	20 (17-27)	20 (14-23)
0-48 h cumulative postoperative morphine consumption, mg	68 (50-91)	86 (59-109)‡	62 (48-87)
Postoperative nausea and vomiting, No. of patients	7	8	8
Droperidol, No. of doses/No. of patients	8/7	8/8	8/8

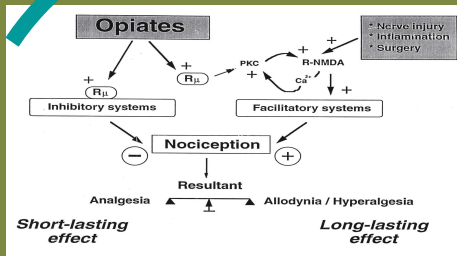


- Trauma chirurgical
- absence d'analgésie préventive

## A- Influx nociceptifs



# Sensibilisation



## B- Opioides

- Anesthésie balancée avec fortes doses d'opioïdes
- Absence de stratégies anti-sensibilisantes

# « Chronicisation »

# *Douleur chronique postopératoire*

## *Chronic Pain as an Outcome of Surgery*

### *A Review of Predictive Factors*

Frederick M. Perkins, M.D.,\* Henrik Kehlet, M.D., Ph.D.†

Anesthesiology 2000; 93:1123-33

**Macrae W.A. Chronic pain after surgery. Meta-analysis.  
BJA 2001**

Pour parler de douleur postopératoire chronique, il faut :

- qu'elle apparaisse après chirurgie
- qu'elle dure depuis au moins 2 mois après acte chirurgical
- les autres causes doivent être exclues (néoplasie évolutive, infection chronique...)...

***5 to 70% des patients présentaient des douleurs  
chroniques après chirurgie***

## Dernière décennie :

<b>Surgery</b>	<b>Incidence (%)</b>	<b>References</b>
Breast	22-56	Wallace et al, 1996
Inguinal hernia	19	Callesen et al, 1999
Inguinal hernia (mesh)	43 (35*)	Nienhuij et al, 2005
CABG	56	Eisenberg et al, 2001
CABG	44	Bar-El et al, 2005
Pelvic trauma	48	Meyhoff et al, 2006
Femoral popliteal bypass	23*	Greiner et al, 2004
Hip arthroplasty	28	Nikolajsen et al, 2006

\* neuropathy

## *Exemple de la chirurgie cardiaque*

- Patients avec douleur chronique après « Coronary Artery Bypass Grafting (CABG) » en Israël :

**56%** (Eisenberg E. et al, Pain 2001) ou **44%** (Bar-El Y. et al, EJCTS 2005)

- Dans les 2 études : altération de la qualité de vie par la douleur chronique : **72%** et **86%** des patients respectivement

## Dysaesthesia associated with sternotomy for heart surgery†

R. P. Alston\* and P. Pechon

*Department of Anaesthesia, Critical Care and Pain Medicine and Department of Cardiothoracic Surgery,  
Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh EH16 4SA, UK*

*\*Corresponding author. E-mail: peter.alston@ed.ac.uk*

Dysesthesies : 27 des 50 patients included = 54%

Littérature: de 40 à 60 % 3 mois après chirurgie

En régression logistique, l'aire d'hyperalgésie était corrélée à  
( $p < 0,01$ ) :

- CABG (versus valve)
- intensité de la douleur post-op



# The incidence of chronic post-sternotomy pain after cardiac surgery – a prospective study

J. MEYERSON<sup>1</sup>, S. THELIN<sup>2</sup>, T. GORDH<sup>1</sup> and R. KARLSTEN<sup>1</sup>

<sup>1</sup>Multidisciplinary Pain Treatment Centre, Department of Anaesthesiology, and Department of Thoracic and <sup>2</sup>Cardiovascular Surgery, University Hospital, Uppsala, Sweden

**318 analyzed questionnaires after one year; pain at sternotomy site one year at rest after surgery = 28%**

**AAS 2001; 45:940-944**

## Persistent Pain After Cardiac Surgery: An Audit of High Thoracic Epidural and Primary Opioid Analgesia Therapies

Sue C. Ho, MBBS, FANZCA\*, Colin F. Royse, MBBS, MD, FANZCA†, Alistair G. Royse, MBBS, MD, FRACStg, Arthur Penberthy, MBBS, FANZCA\*, and Roderick McRae, MBBS, FANZCA, FANZCA†

**244 analyzed questionnaires; pain at sternotomy 2 months after surgery = 25%**

**Anesth Analg 2002;95:820-3**

## *Pain after Cardiac Surgery*

*A Prospective Cohort Study of 1-Year Incidence and Intensity*

Pasi Lahtinen, M.D.,\* Hannu Kokki, M.D., Ph.D.,† Markku Hynynen, M.D., Ph.D.‡

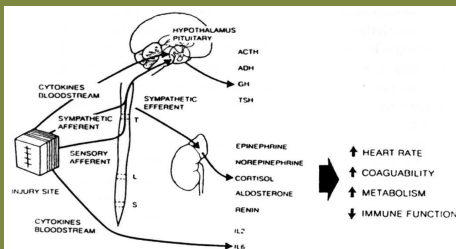
**186 analyzed questionnaires after one year; pain at sternotomy site one year at rest after surgery = 14% ; upon movement = 31%**

**Anesthesiology 2006; 105:794-800**

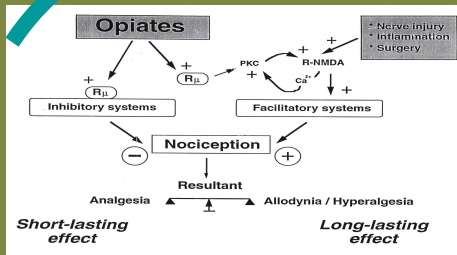
**Comment traiter vite et bien  
une douleur aiguë ?**

- Trauma chirurgical : « je réduis la lésion! »
- Analgésie multimodale « préventive » + ttt antisensibilisante

## A- Influx nociceptifs



# Sensibilisation



## B- Opioides

# « Chronicisation »

- Anesthésie balancée avec faibles doses d'opioïdes
- Associations à des stratégies anti-sensibilisantes

# Pre-emptive analgesia

???

British Medical Bulletin 2004; 71: 13-27

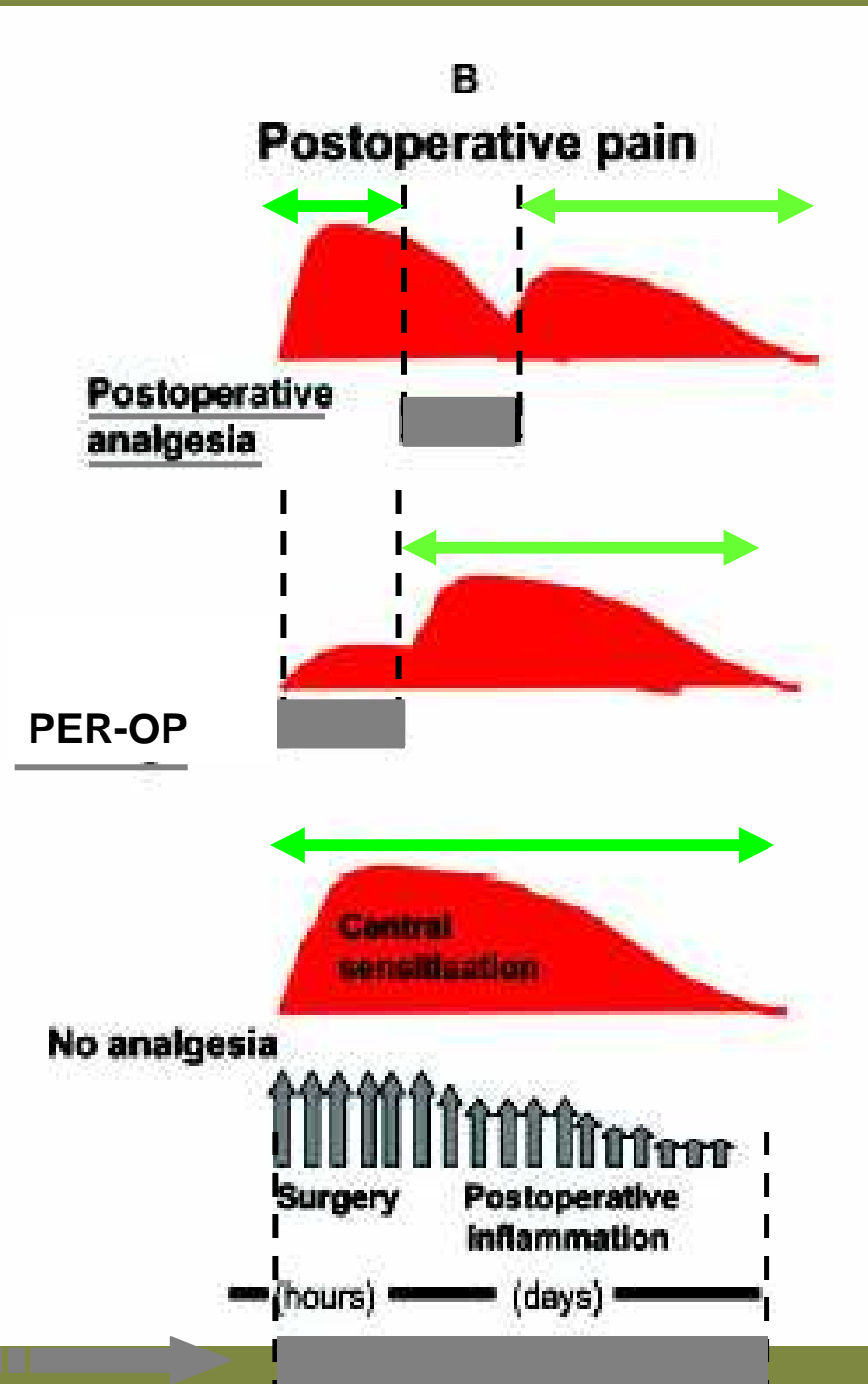
Jørgen B. Dahl and Steen Møiniche

Department of Anaesthesiology, Glostrup University Hospital, Glostrup, Denmark

« La seule façon de prévenir la sensibilisation centrale serait de bloquer complètement toute douleur émanant du site chirurgical depuis le moment de l'incision jusqu'à la guérison totale »



Analgesie multimodale idéale



# Stratégies thérapeutiques

**Analgésie optimale :**  
**Paracétamol**  
**AINS**  
**Nefopam**  
**ALR...**

**Du nouveau???**

# Paracétamol et Anti-sensibilisation : OUI !

Acetaminophen blocks spinal hyperalgesia induced by  
NMDA and substance P

R. Bkörkman, K. Hallman, J. Hedner, T. Hedner and M. Henning  
Gothenburg, Sweden

Pain 1994; 57 (3): 259-64

The dose-related effects of paracetamol on hyperalgesia  
and nociception in the rat

M. Bianchi, A.E. Panerai

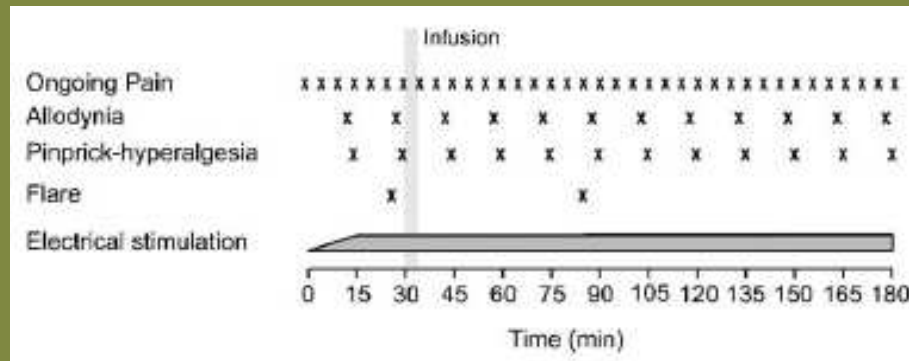
Br J Pharmacol 1996 Jan; 117 (1): 130-2

3 doses de paracétamol sur inflammation par carragénine : 25, 50, 100mg/kg PO  
Réduction de l'hyperalgésie post-inflammation (seuil nociceptif)  
Effet central : diminue aussi l'hyperalgésie contro-latérale  
Pas d'effet sur l'inflammation de la patte injectée

# The cyclooxygenase isozyme inhibitors parecoxib and paracetamol reduce central hyperalgesia in humans

Wolfgang Koppert<sup>a,\*</sup>, Andreas Wehrfritz<sup>a</sup>, Nicole Körber<sup>a</sup>, Reinhard Sittl<sup>a</sup>,  
Sven Albrecht<sup>a</sup>, Jürgen Schüttler<sup>a</sup>, Martin Schmelz<sup>b</sup>

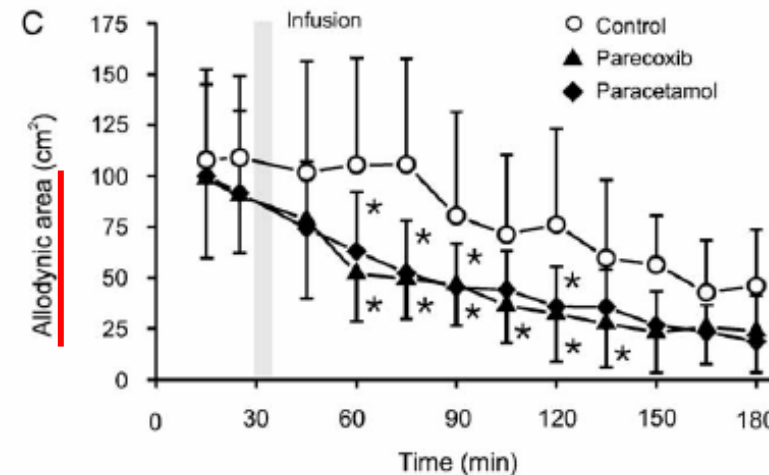
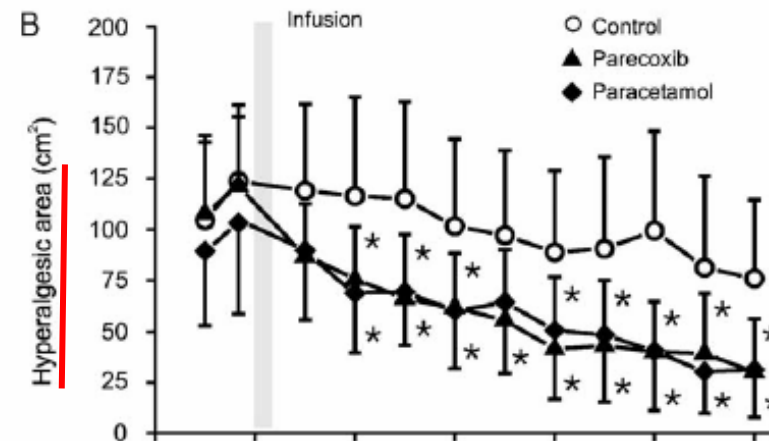
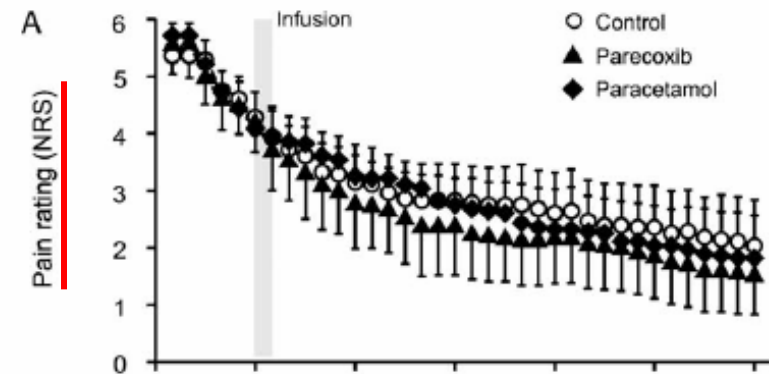
Pain 108 (2004) 148–153



## Volontaire sains

Modèle d'hyperalgésie induite par stimulation électrique cutanée

Le paracétamol limite le développement d'hyperalgésie et d'allodynie





# Analgesie et Implication des récepteurs HT

Serotonin receptor subtypes involved in the spinal antinociceptive effect of 5-HT in rats

Laurent Bardin, Jeannine Lavarenne, Alain Eschalier\*

Pain 86 (2000) 11-18

## *The Role of 5-HT<sub>1A/B</sub> Autoreceptors in the Antinociceptive Effect of Systemic Administration of Acetaminophen*

Arénzazu Roca-Vinardell, Pharm. B.Sc.,\* Antonio Ortega-Alvero, Ph.D.,† Juan Gilbert-Rahola, Ph.D.,‡ Juan A. Micó, Ph.D.‡

Anesthesiology 2003; 98:741-7

Roles of serotonin receptor subtypes for the antinociception of 5-HT in the spinal cord of rats

Chang Young Jeong, Jeong Il Choi, Myung Ha Yoon\*

European Journal of Pharmacology 502 (2004) 205-211

Spinal 5-HT<sub>1A</sub> receptors differentially influence nociceptive processing according to the nature of the noxious stimulus in rats: effect of WAY-100635 on the antinociceptive activities of paracetamol, venlafaxine and 5-HT

Jérôme Bonnefont<sup>a</sup>, Eric Chapuy<sup>a</sup>, Eric Clottes<sup>b</sup>, Abdelkrim Alloui<sup>a</sup>, Alain Eschalier<sup>a,\*</sup>

Pain 114 (2005) 482-490

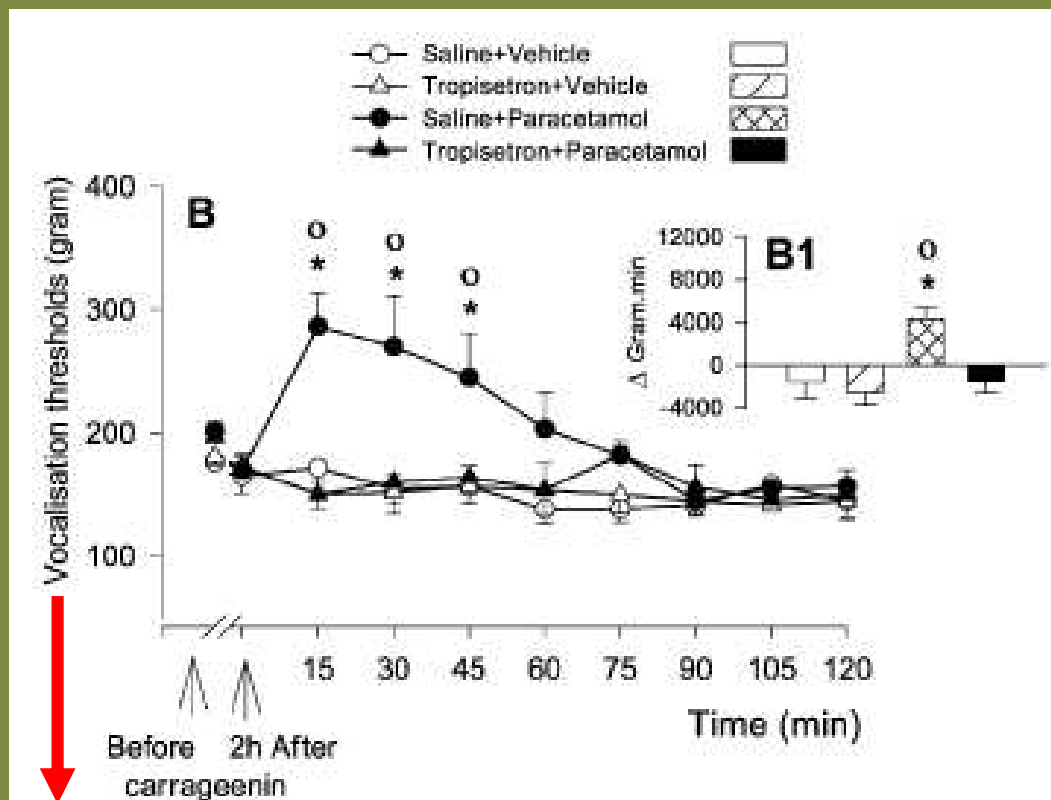
# Paracetamol exerts a spinal, tropisetron-reversible, antinociceptive effect in an inflammatory pain model in rats

Abdelkrim Alloui<sup>a,\*</sup>, Claude Chassaing<sup>a</sup>, Jeannot Schmidt<sup>a</sup>, Denis Ardid<sup>a</sup>, Claude Dubray<sup>a</sup>,  
Alix Cloarec<sup>b</sup>, Alain Eschalier<sup>a</sup>

<sup>a</sup>EMI INSERM/Uda 9904, Laboratoire de Pharmacologie Médicale, Faculté de Médecine, BP 38, 63001 Clermont-Ferrand Cedex 1, France

<sup>b</sup>Laboratoires UPSA/BMS, Grande Arche La Défense, Paris, France

Received 20 December 2001; received in revised form 22 March 2002; accepted 26 March 2002



Action analgésique centrale :  
action par récepteurs 5HT-3

Pas d'action anti-  
inflammatoire



Association aux  
AINS recommandée

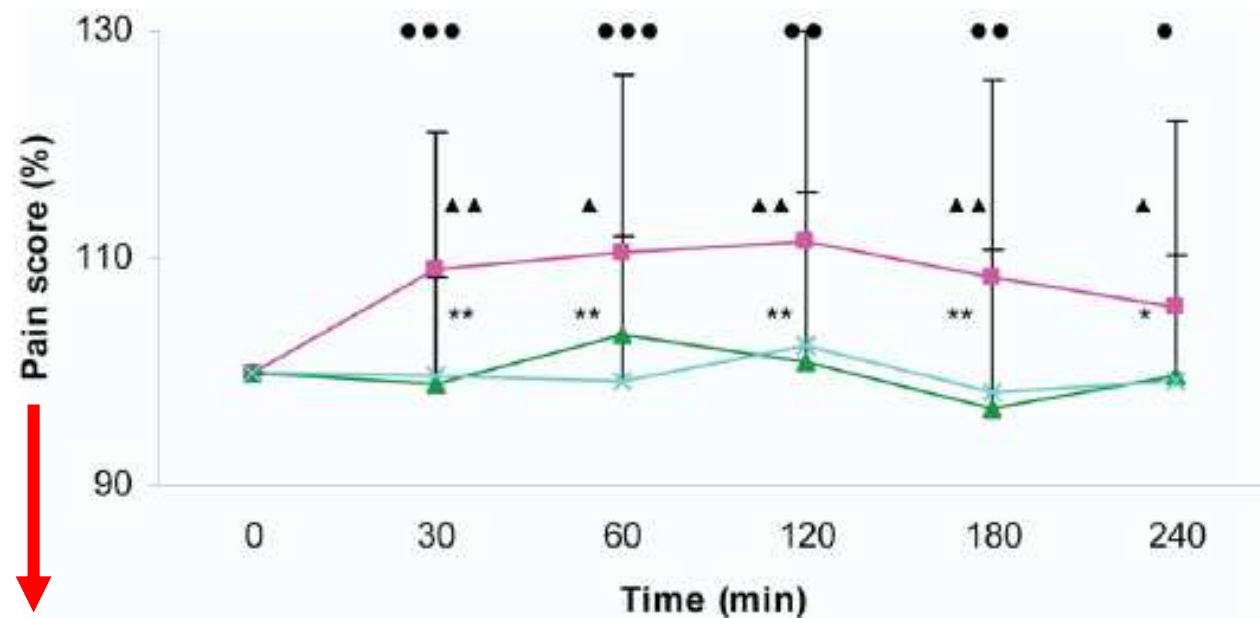
Réponse douloureuse à une  
stimulation mécanique

Etude animale (rats)

# Analgesic effect of acetaminophen in humans: First evidence of a central serotonergic mechanism

Gisèle Pickering, MD, Marie-Anne Lorient, Pharm, PhD, Frédéric Libert, MPharm, Alain Eschaliér, MD, Philippe Beaune, Pharm, PhD, and Claude Dubray, MD *Clermont-Ferrand and Paris, France*

*Acetaminophen in humans: A serotonergic mechanism*



APAP/Pl

Acet.1g PO  
/placebo

APAP/Tr

Acet. 1g PO  
/tropisetron

APAP/Gr

Acet.1g PO  
/granisetron

Réponse douloureuse à une  
stimulation électrique

Volontaires sains

CLINICAL PHARMACOLOGY & THERAPEUTICS

APRIL 2006

# Analgesic efficacy and safety of intravenous paracetamol (acetaminophen) administered as a 2 g starting dose following third molar surgery

Gitte I. Juhl <sup>a,\*</sup>, Sven E. Norholt <sup>b</sup>, Else Tonnesen <sup>c</sup>, Odile Hiesse-Provost <sup>d</sup>,  
Troels S. Jensen <sup>a</sup>

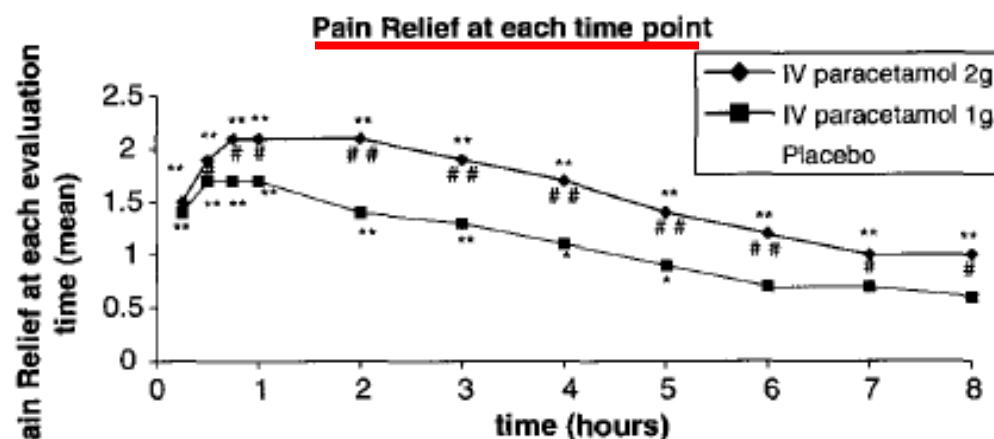
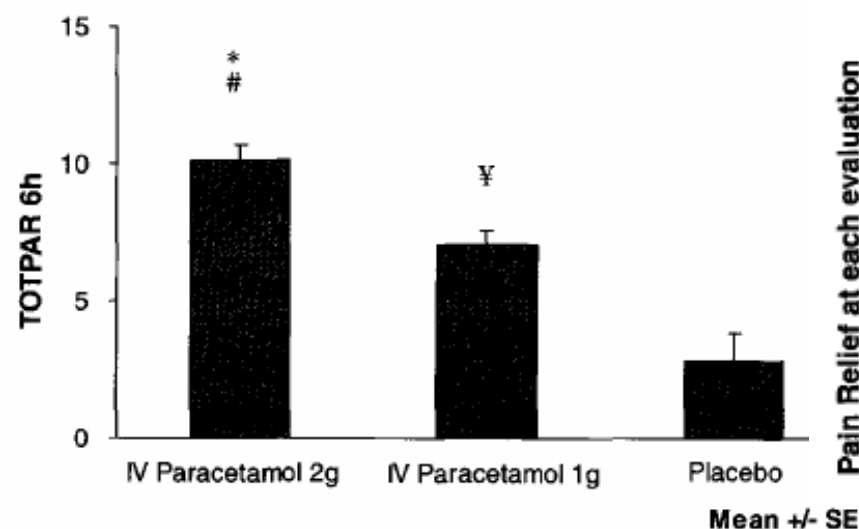
<sup>a</sup> Danish Pain Research Centre, Aarhus University Hospital, Norrebrogade 44, 8000 Aarhus C, Denmark

<sup>b</sup> Department of Oral and Maxillofacial Surgery, Aarhus University Hospital, Denmark

<sup>c</sup> Department of Anesthesia, Aarhus University Hospital, Denmark

<sup>d</sup> Medical Department, Bristol-Myers Squibb, 92500 Rueil Malmaison, France

European Journal of Pain 10 (2006) 371–377



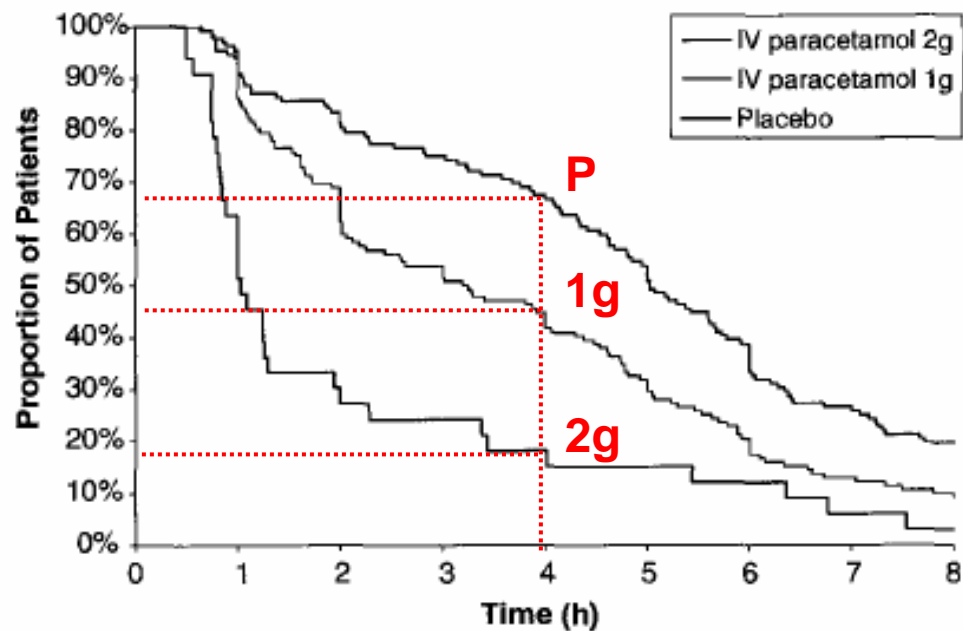


Fig. 3. Time to rescue medication.

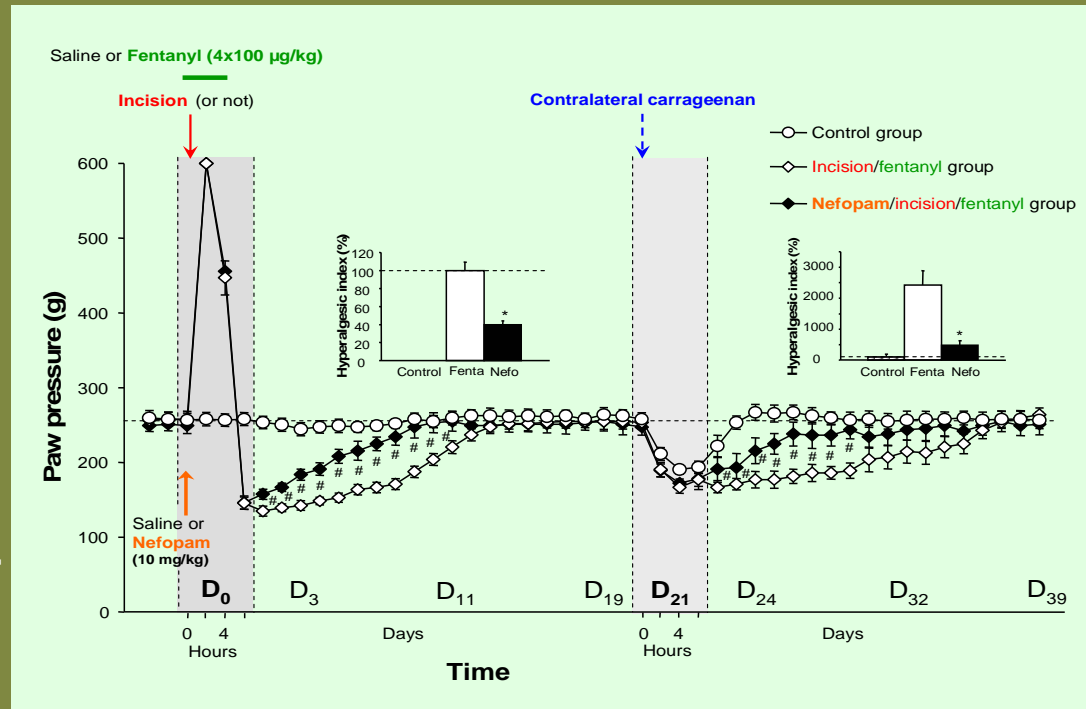
**Adverse events**

Adverse event <i>N</i> (%)	IV APAP <sup>a</sup> 2 g	IV APAP 1 g	Placebo	Overall comparison <i>p</i>
Patients with at least one adverse event	75 (56.8)	80 (60.6)	18 (54.5)	0.7413
Patients with at least one related adverse event	2 (1.5)	2 (1.5)	1 (3.0)	0.6520
Total number of adverse events reported	151	181	35	
Adverse events reported by more than 10% of patients				
Fatigue	20 (15.2)	16 (12.1)	4 (12.1)	<b>NS</b>
Surgical site reaction	16 (12.1)	24 (18.2)	1 (3.0)	
Headache	14 (10.6)	16 (12.1)	2 (6.1)	
Postoperative hemorrhage	12 (9.1)	13 (9.8)	5 (15.2)	
Operation site inflammation	7 (5.3)	12 (9.1)	5 (15.2)	

<sup>a</sup> APAP = paracetamol.

# Néfopam

Paw pressure vocalization test



- Nefopam opposed the long-lasting hyperalgesia induced by incisional pain in fentanyl-treated rats

- Nefopam reduced pain vulnerability observed for a long while after the prior painful event

## The Effect of Nefopam on Morphine Overconsumption Induced by Large-Dose Remifentanil During Propofol Anesthesia for Major Abdominal Surgery

Myriam Tirault, MD\*, Nicolas Derrode, MD\*, David Clevenot, MD\*, Delphine Rolland, MD\*, Dominique Fletcher, MD†, and Bertrand Debaene, MD\*

\*Department of Anesthesiology and Intensive Care, Hôpital J. Bernard, Poitiers, France; †Department of Anesthesiology and Intensive Care, Hôpital R. Poincaré, Garches, France

Opioids may activate pain facilitatory systems opposing analgesia. We investigated whether large-dose remifentanil given during IV anesthesia caused postoperative morphine overconsumption and whether nefopam (a centrally acting analgesic) could reduce this. Sixty patients scheduled for abdominal surgery were included in this prospective, randomized study. The first 30 patients received either small-dose (Group S: 3 ng/mL) or large-dose (Group L: 8 ng/mL) remifentanil administered by a target-controlled infusion during propofol anesthesia. Before skin closure, patients received morphine 0.15 mg/kg. Another 30 patients also received nefopam 20 mg intraoperatively. Postoperative pain was controlled by titration of morphine, followed by patient-controlled morphine analgesia

(PCA). Morphine was requested earlier in Group L than in Group S (10 [1–63] min versus 37 [5–90] min, median [range];  $P < 0.002$ ). The dose of morphine by titration was larger in Group L than in Group S (0.28 [0.04–0.38] mg/kg versus 0.16 [0.03–0.41] mg/kg;  $P < 0.05$ ). PCA morphine consumption and pain scores were similar. There were no differences between the nefopam groups in the time to first morphine request or in the dose of morphine by titration. Postoperative morphine overconsumption occurred after large-dose remifentanil and propofol anesthesia during the early postoperative period. Pretreatment with nefopam could be useful to prevent pain sensitization induced by opioids.

(Anesth Analg 2006;102:110–7)

# Stratégies antisensibilisantes



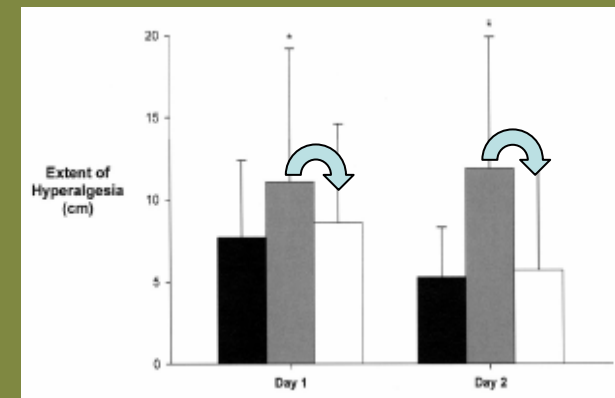
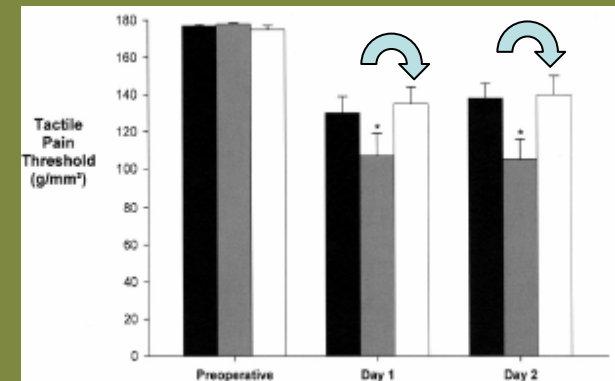
# Remifentanyl-induced Postoperative Hyperalgesia and Its Prevention with Small-dose Ketamine

Vincent Joly, M.D.,\* Philippe Richebe, M.D.,† Bruno Guignard, M.D.,\* Dominique Fletcher, M.D.,‡ Pierre Maurette, M.D.,§ Daniel I. Sessler, M.D.,|| Marcel Chauvin, M.D.#

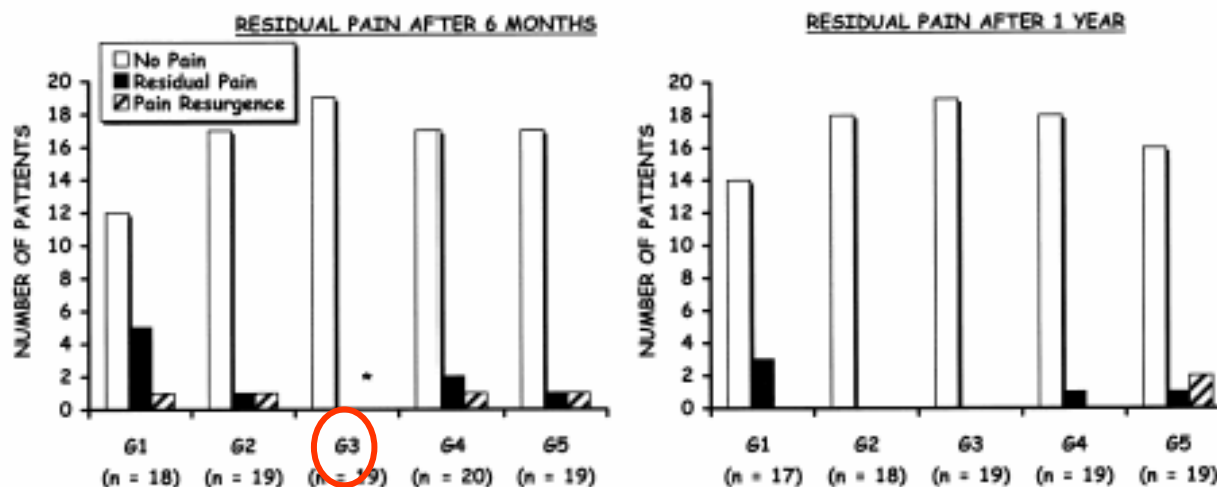
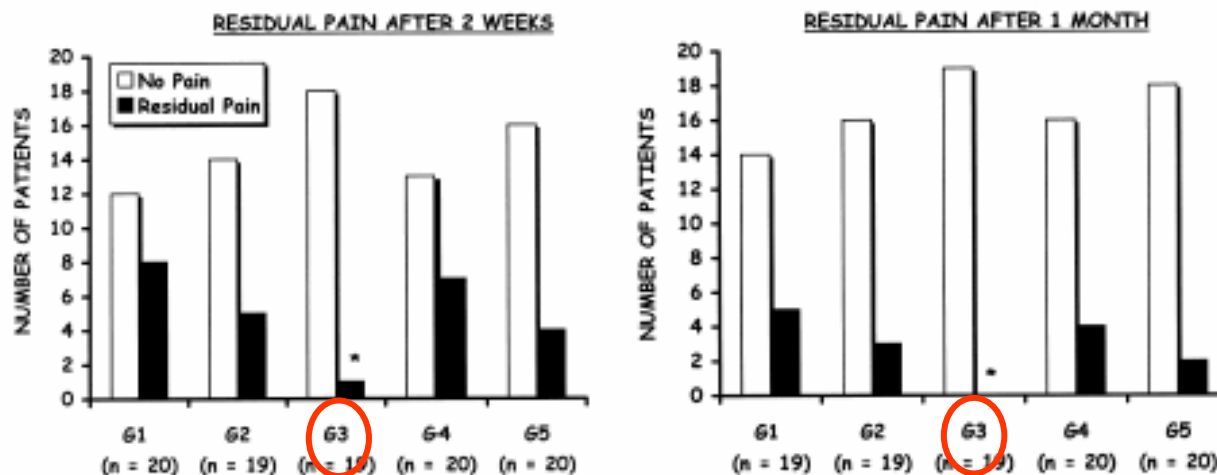
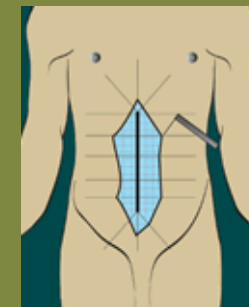
	Small-dose Remifentanyl (n = 25)	Large-dose Remifentanyl (n = 25)	Large-dose Remifentanyl-Ketamine (n = 24)
Remifentanyl dose, mg	0.9 ± 0.3*	6.7 ± 3.1	6.5 ± 3.4
Desflurane, MAC/h	0.8 ± 0.2*	0.5 ± 0.2	0.6 ± 0.2
Ephedrine, No. of doses/No. of patients	9/17	10/13	50/15†
Final intraoperative temperature, °C	36.6 ± 0.7	36.3 ± 0.8	36.3 ± 0.9
Awakening time, min	14 ± 6	13 ± 5	14 ± 6
Extubation time, min	16 ± 6	14 ± 6	15 ± 4
Time to first postoperative morphine, min	35 (28-46)	24 (20-33)	41 (32-52)
Morphine given in PACU, mg	16 (10-24)	20 (17-27)	20 (14-23)
0-48 h cumulative postoperative morphine consumption, mg	68 (50-91)	86 (59-109)‡	62 (48-87)
Postoperative nausea and vomiting, No. of patients	7	8	8
Droperidol, No. of doses/No. of patients	8/7	8/8	8/8



**Ketamine**  
=  
**moins d'hyperalgésie**



# Intérêt dans la chronicisation des DPO



G1 = CONTROL  
 G2 = LOW DOSE KETAMINE IV  
 G3 = HIGH DOSE KETAMINE IV  
 G4 = LOW DOSE KETAMINE EPI  
 G5 = HIGH DOSE KETAMINE EPI

De Kock M. and al.  
 Pain, 2001. 92: 373-80

## Ketamine and postoperative pain – a quantitative systematic review of randomised trials

Nadia Elia\*, Martin R. Tramèr *Pain* 113 (2005) 61–70

*EBCAP Institute (Evidence-Based Critical care, Anaesthesia and Pain treatment), Division of Anaesthesiology, Geneva University Hospitals, 24 Rue Micheli-du-Crest, CH-1211 Geneva 14, Switzerland*

Received 5 May 2004; received in revised form 10 September 2004; accepted 28 September 2004

## Peri-operative ketamine for acute post-operative pain: a quantitative and qualitative systematic review (Cochrane review)

*Acta Anaesthesiol Scand* 2005; 49: 1405–1428  
Printed in UK. All rights reserved

R. F. BELL<sup>1</sup>, J. B. DAHL<sup>2</sup>, R. A. MOORE<sup>3</sup> and E. KALSO<sup>4</sup>

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## *Ketamine for Perioperative Pain Management*

Sabine Himmelseher, M.D.,\* Marcel E. Durieux, M.D., Ph.D.†

*Anesthesiology* 2005; 102: 211–20

etc....

# Le protoxyde d'azote



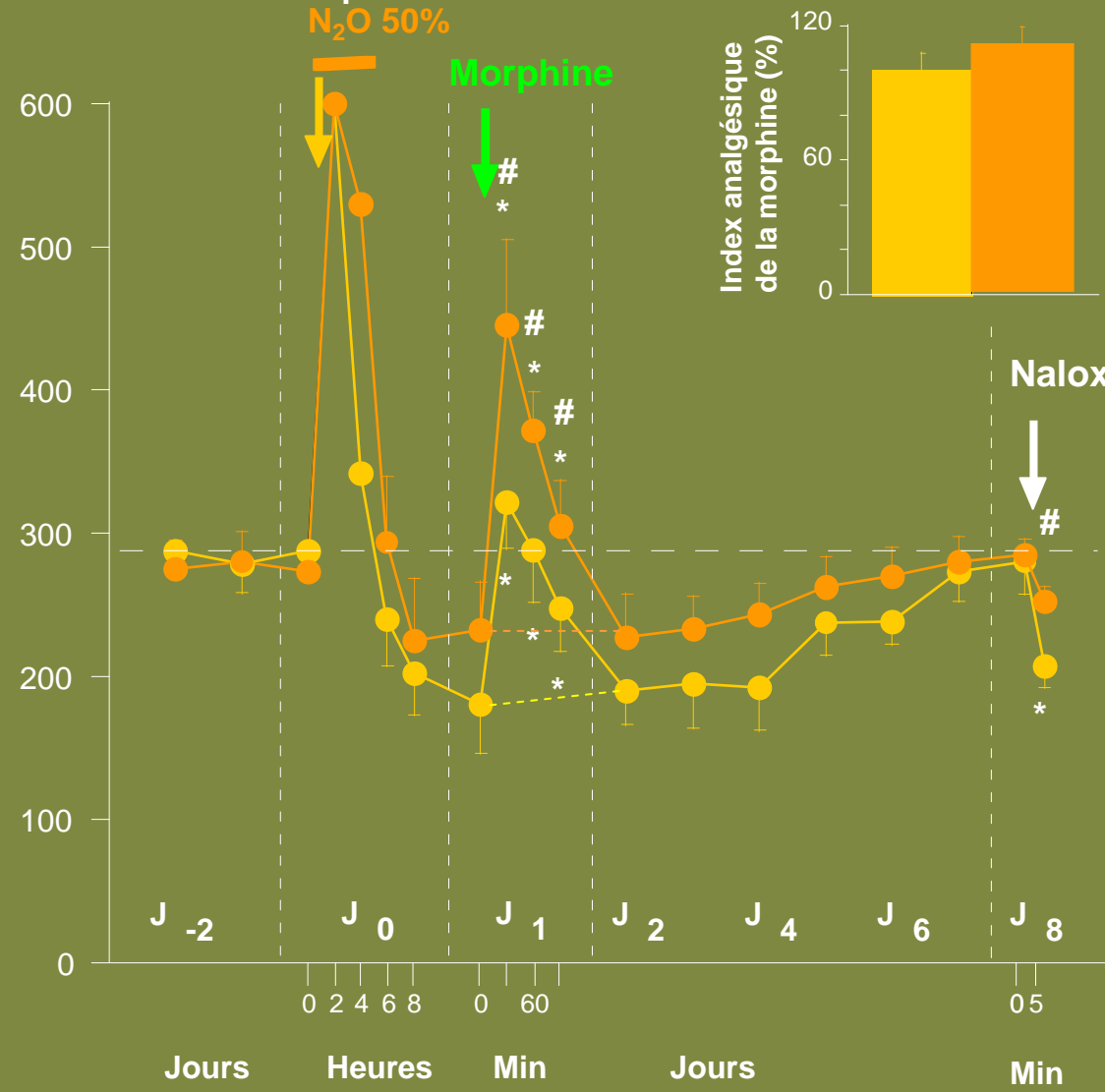
# 50%

Fentanyl  
+  
Incision

+  
N<sub>2</sub>O 50%

Morphine

Pression patte postérieure (g)

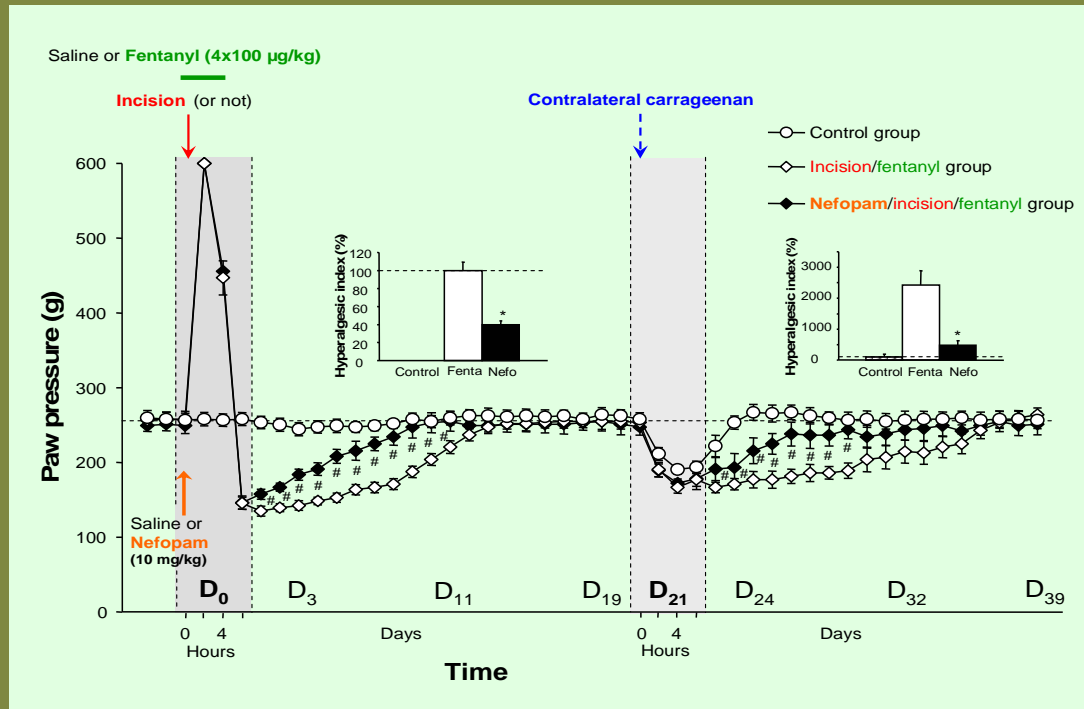


Naloxone

Temps

# Néfopam

Paw pressure vocalization test



- Nefopam opposed the long-lasting hyperalgesia induced by incisional pain in fentanyl-treated rats

- Nefopam reduced pain vulnerability observed for a long while after the prior painful event

# Gabapentine, pregabaline

## Où agissent-elles?

- Niveau Supraspinal : *Singh et al, Psychopharmacology 1996*
- Corne Dorsale, 2<sup>nd</sup> neurone: *Shimoyama et al, Pain 2000*
- Dorsal root ganglia (DRG) : *Sutton et al, B J Pharmacol 2002*
- A delta : *Werner et al, Reg Anesth Pain Med 2001*
- A alpha, A beta : *Hanesh et al, Pain 2003*
- Fibres C : *Carlton et al, Pain 1998*

## Comment agissent-elles?

- sur les sous-unités  $\alpha 2\delta$  des canaux calciques type N du DRG = action la plus probable
- diminution du  $Ca^{++}$  entrant => réduction de la transmission de l'influx nociceptifs

*Gee et al. J biol Chem 1996*

*Sutton et al. Br J Pharmacol 2002*

*Cheng et al. Anesth Analg 2006*

## Gabapentine, pregabalin

### The Analgesic Effects of Perioperative Gabapentin on Postoperative Pain: A Meta-Analysis

Robert W. Hurley, M.D., Ph.D., Steven P. Cohen, M.D.,  
Kayode A. Williams, M.D., Andrew J. Rowlingson, B.A., and  
Christopher L. Wu, M.D.

*Regional Anesthesia and Pain Medicine, Vol 31, No 3 (May–June), 2006: pp 237–247*

**Conclusions:** Based on this systematic review, perioperative oral gabapentin is a useful adjunct for the management of postoperative pain that provides analgesia through a different mechanism than opioids and other analgesic agents and would make a reasonable addition to a multimodal analgesic treatment plan. *Reg Anesth Pain Med 2006;31:237-247.*



## Regional Anesthesia and Pain

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### Preoperative gabapentin for postoperative analgesia: a meta-analysis

*[L'administration préopératoire de gabapentine pour l'analésie postopératoire:  
une méta-analyse]*

Rachael K. Seib MA,\* James E. Paul MD MSc FRCPC†

CAN J ANESTH 2006 / 53: 5 / pp 461-469

**Conclusion:** Although gabapentin given preoperatively decreases pain scores and analgesic consumption in the first 24 hr after surgery, the clinical significance of this finding has yet to be determined. This meta-analysis could not demonstrate a significant reduction in the incidence of side effects. Due to the small numbers enrolled in the studies, larger randomized control trials are warranted.

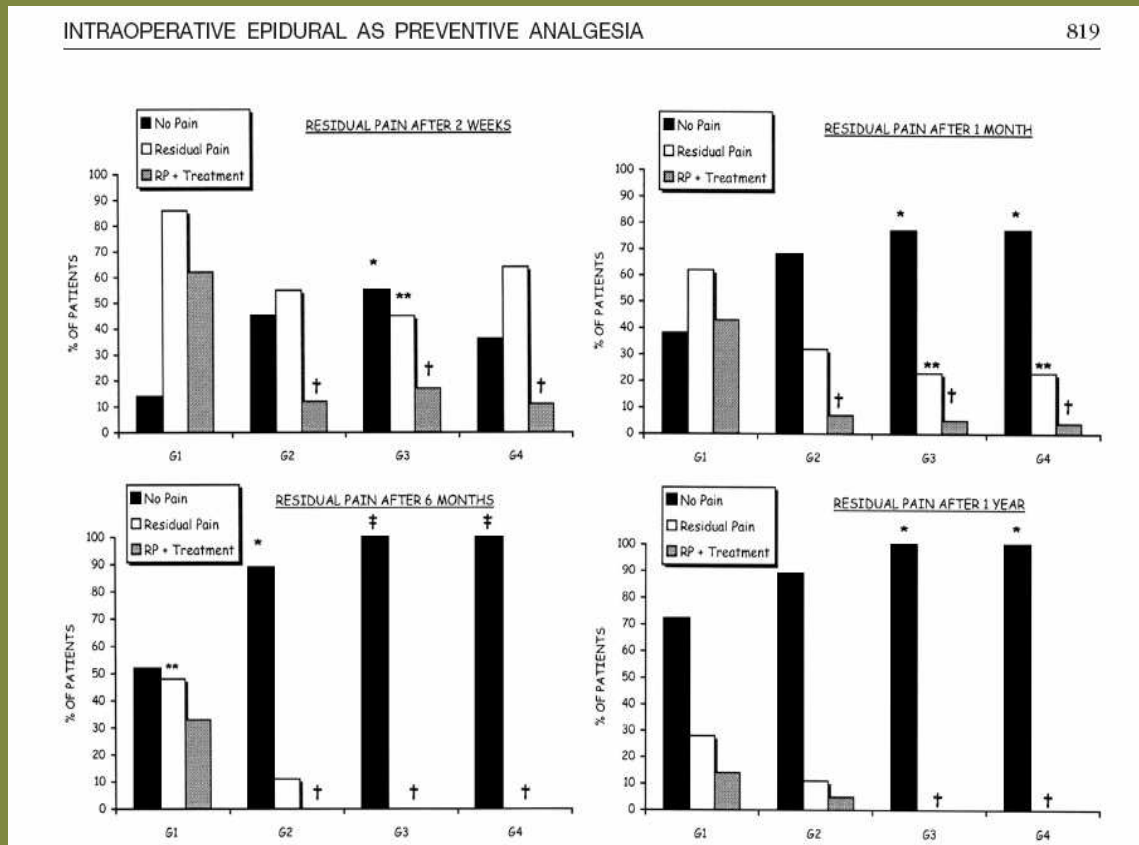
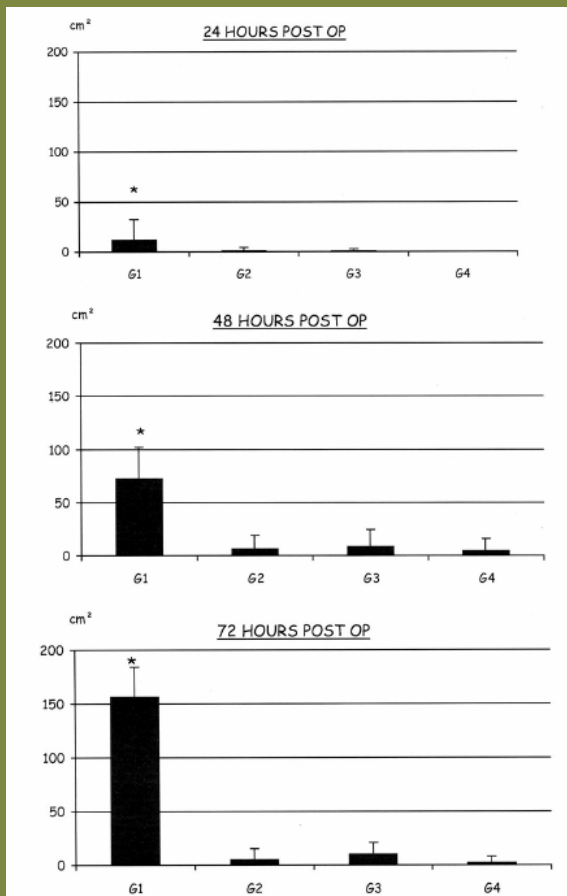
# Stratégies combinées = perspectives!!! ????

Anesthesiology 2005; 103:813-20

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## Intraoperative Epidural Analgesia Combined with Ketamine Provides Effective Preventive Analgesia in Patients Undergoing Major Digestive Surgery

Patricia Lavand'homme, M.D., Ph.D.,\* Marc De Kock, M.D., Ph.D.,† Hilde Waterloos, R.N.‡



# Conclusion

- Sensibilisation périphérique et centrale ont des **substratum physiologiques** mieux connus de nos jours
- Traiter la douleur aiguë postopératoire = limiter le risque de chronicisation!
- De **nombreuses cibles thérapeutiques** existent donc pour limiter la sensibilisation
- Les stratégies thérapeutiques actuelles doivent associer **analgésie multimodale** et **anti-hyperalgésiques**

# PREVENTIVE analgesia → ???

British Medical Bulletin 2004; 71: 13-27

Jørgen B. Dahl and Steen Møiniche

Department of Anaesthesiology, Glostrup University Hospital, Glostrup, Denmark

« La seule façon de prévenir la sensibilisation centrale serait de bloquer complètement toute douleur émanant du site chirurgical depuis le moment de l'incision jusqu'à la guérison totale »



Analgesie multimodale idéale

