

*Il n'y a pas de douleurs,  
il n'y a que des hommes douloureux...*

**Guy Simonnet**

**Equipe « Homéostasie – Allostasie – Pathologie – Réhabilitation »**

**CNRS UMR 5287**

**Université de Bordeaux**

**HAPR**  
Bx2-CNRS  
UMR 5287

**CapDouleur, Lyon, 27 Novembre 2019**

Pas de conflit d'intérêts

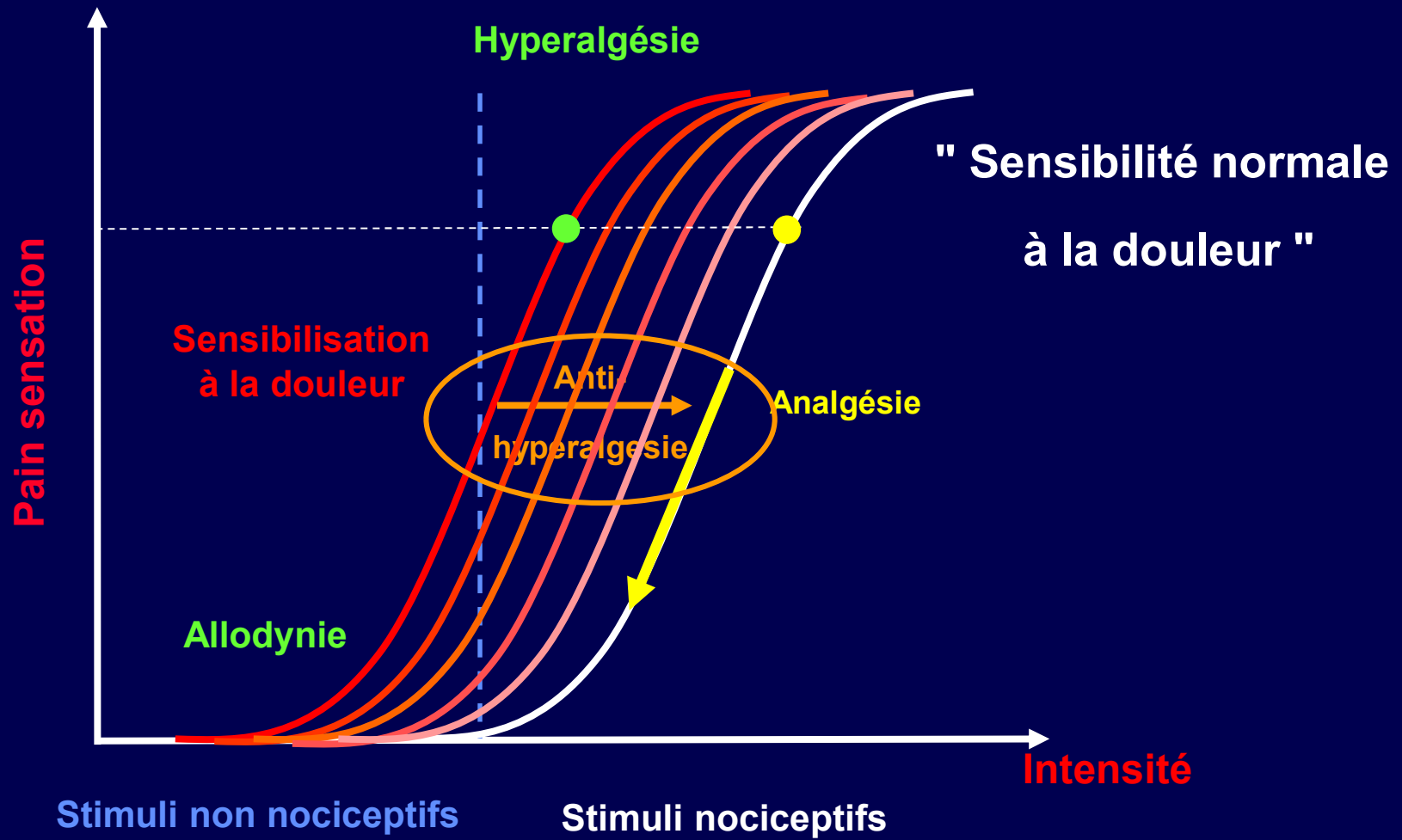
# Epidémiologie et coût des douleurs chroniques

- 43% des consultations en France ont un motif douleur ( > 10 millions de français affectés de douleurs chroniques)
- Un européen sur 5 (19%) souffre de douleurs chroniques
  - 21% des européens atteints de douleur chronique sont totalement incapables de travailler en raison de leur douleur
  - 38% des personnes souffrant de douleurs chroniques indiquent que la douleur n'est pas gérée de manière adéquate
- 10 à 50% des patients opérés ont des douleurs persistantes
- 61% des patients opérés ont des douleurs anormales > 1 an après une thoracotomie
- Coût des douleurs chroniques:
  - 560-635 milliards de dollars/an aux USA (116 millions d'américains) in Relieving Pain in America (2011)
  - 275-550 milliards d'euros en Europe (1.5 à 3% du PIB) in: « Pain proposal », European report (2010); 88 millions de journées de travail en France



> au coût de l'ensemble des syndromes neurologiques

# Niveau de sensation douloureuse



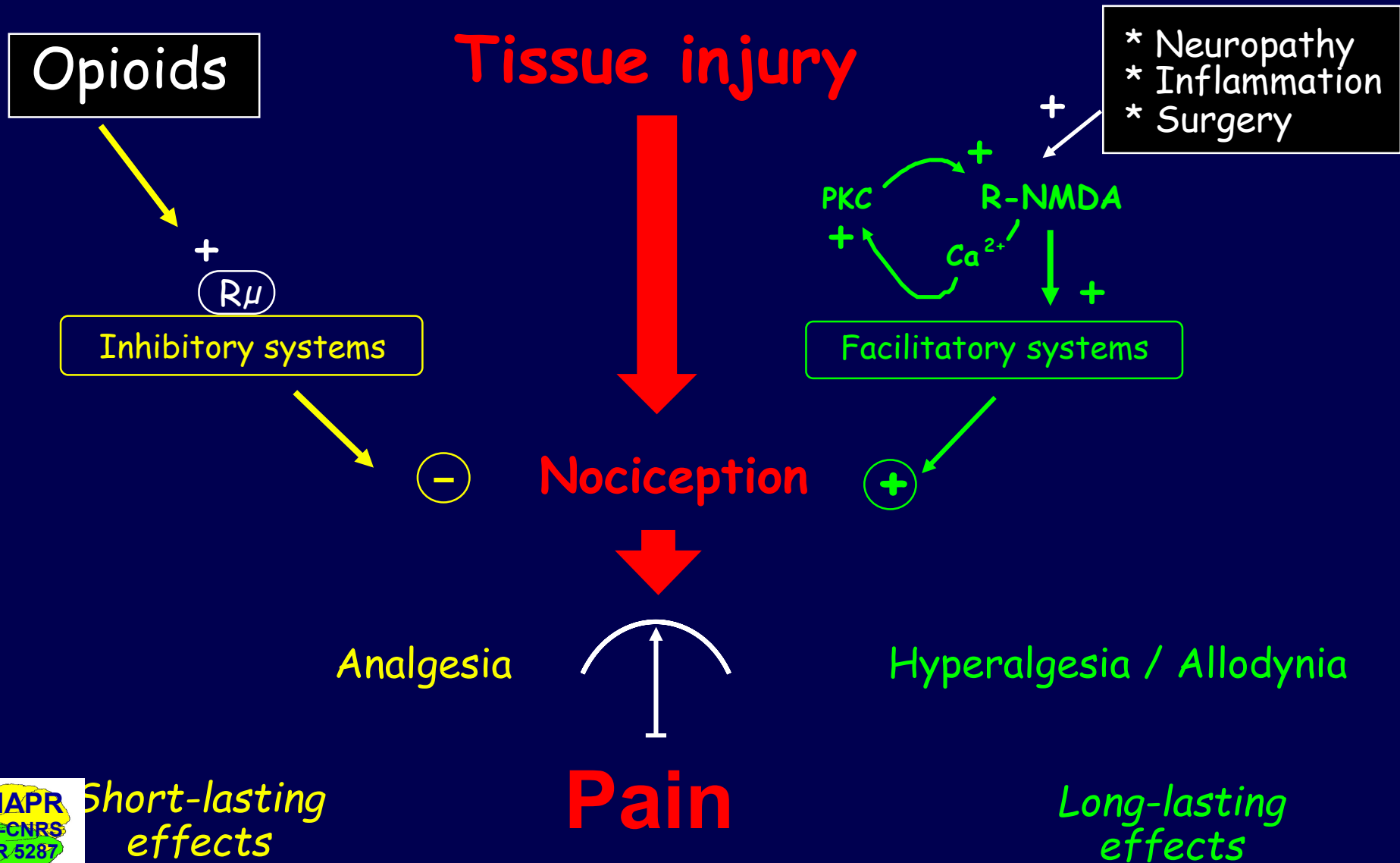
Distinguer et ne pas confondre...

Douleur

et

Sensibilisation à la douleur

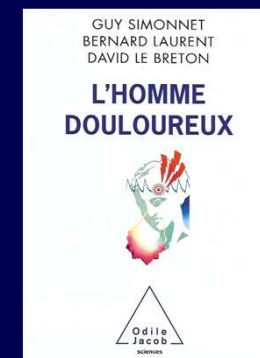
La douleur: un équilibre entre  **systèmes inhibiteurs**   
et  
 **systèmes facilitateurs**



*« La douleur ne s'élabore pas au sein d'un cerveau amnésique, mais au sein d'un système nerveux central imprégné par son passé, qu'il soit récent ou plus lointain.*

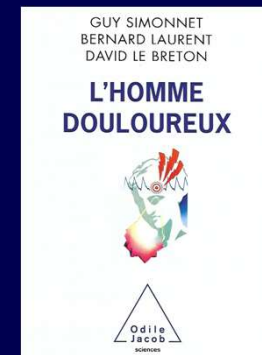
*La mémoire de ce passé concerne l'individu dans son ensemble ainsi que ses relations avec le monde extérieur, mais c'est la mémoire du corps qui constitue le socle sur lequel se bâtit la douleur présente »*

*Daniel Le Bars*



*La douleur est un langage dont l'expression n'est pas toujours consciente, elle est un détour pour dire les souffrances de l'existence sur un mode que les autres peuvent entendre mais qui simultanément devient un piège qui se renferme sur l'individu...*

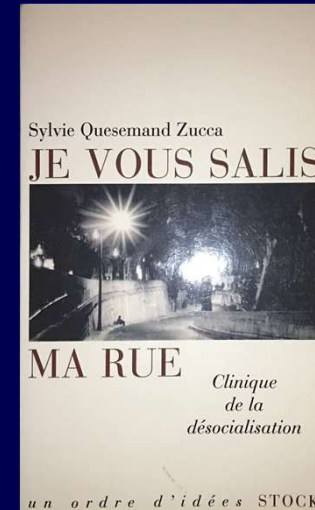
*Dans certaines circonstances, la douleur peut être une sauvegarde venant le protéger de menaces qu'il n'est plus en mesure de repousser...*





# Quand la douleur n'a plus d'adresse...

(SAMU social: Sylvie Zucca et Xavier Emmanuelli)



*Pour ressentir la douleur, il faut nécessairement et  
avant tout exister...*

# Plan

## Comment devient-on douloureux ?

1. Lésion (*pain disease*)
2. Histoire individuelle (*pain illness*)
  - 2.1. douloureuse
  - 2.2. non douloureuse
  - 2.3. pharmacologique
3. Interactions sociales (*compagnonnage*)  
(*pain sickness*)

# Plan

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2. Histoire individuelle (*pain illness*)

2.1. douloureuse

2.2. non douloureuse

2.3. pharmacologique

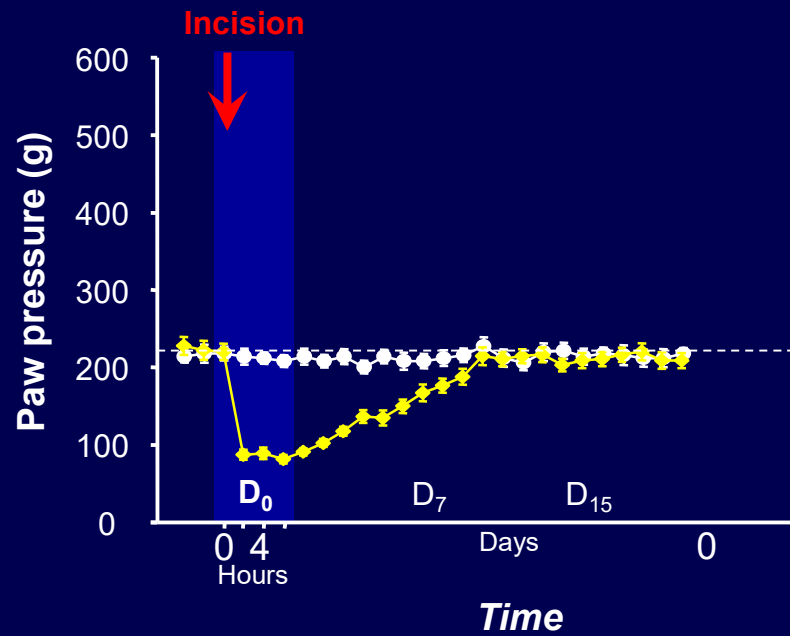
3. Interactions sociales (*compagnonnage*)  
(*pain sickness*)

# Paw pressure vocalization test

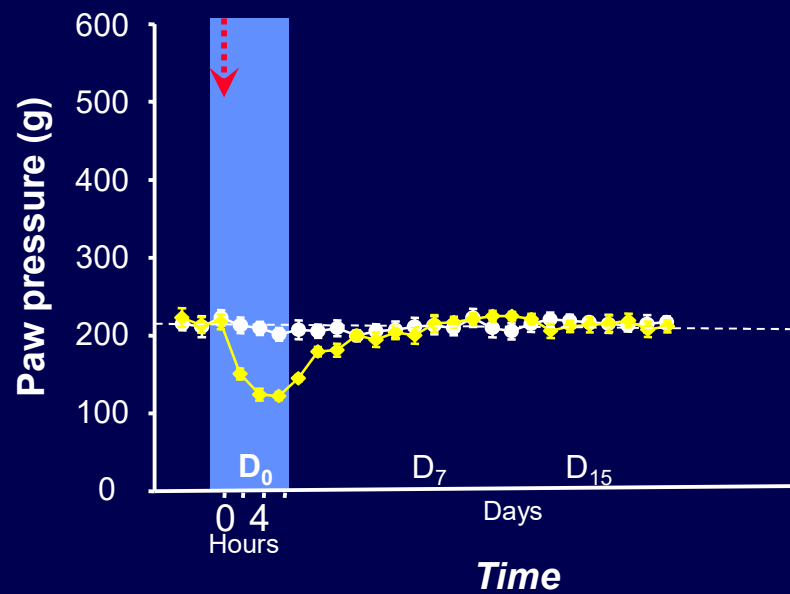
● Control group

◆ Incision group

*Patte lésée*



*Patte non lésée*



# Plan

## Comment devient-on douloureux ?

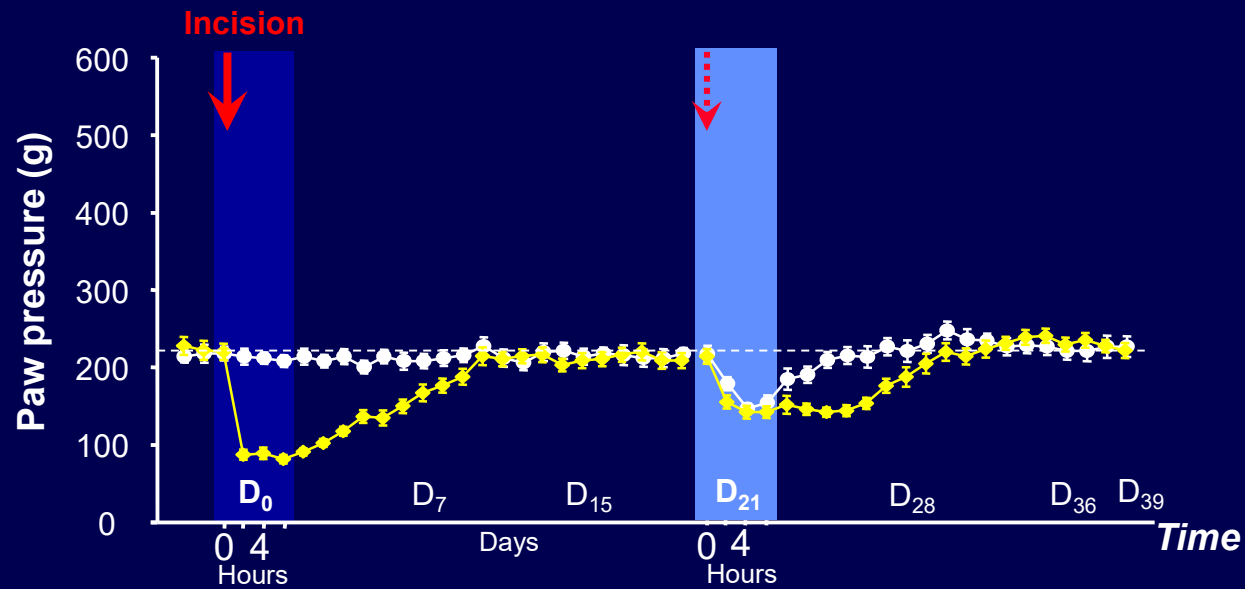
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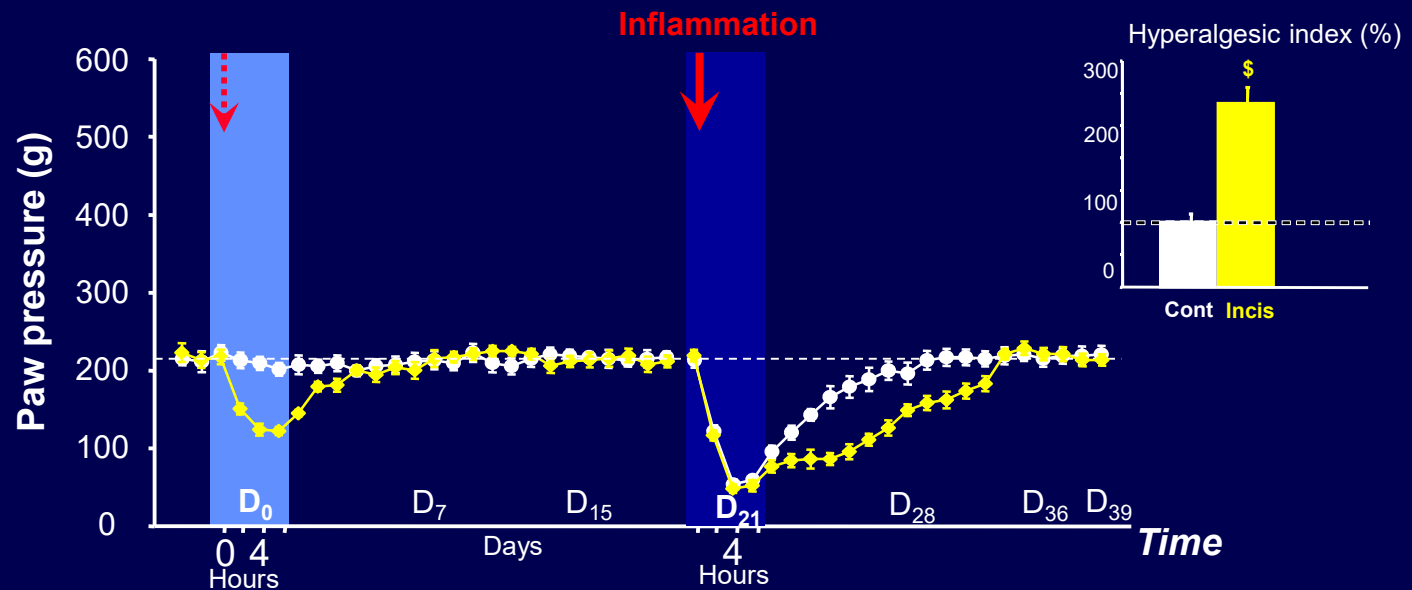
● Control group

◆ Incision group

*Patte lésée*



*Patte non lésée*



## Effect of neonatal circumcision on pain response during subsequent routine vaccination

Anna Taddio, Joel Katz, A Lane Ilersich, Gideon Koren

**Interpretation** Circumcised infants showed a stronger pain response to subsequent routine vaccination than uncircumcised infants. Among the circumcised group, preoperative treatment with Emla attenuated the pain response to vaccination. We recommend treatment to prevent neonatal circumcision pain.

*Lancet* 1997; **349**: 599–603

**Department of Paediatrics, Hospital for Sick Children** (A Taddio MSc, Prof G Koren MD); **Department of Psychology, Toronto Hospital** (J Katz PhD); **and Faculty of Pharmacy** (A Taddio), **Departments of Behavioural Science and Anaesthesia** (J Katz), **and Health Administration** (A L Ilersich MSc), **and Department of Paediatrics and Faculty of Medicine** (G Koren), **University of Toronto, Ontario, Canada**

**Correspondence to:** Prof Gideon Koren, Division of Clinical Pharmacology and Toxicology, Department of Paediatrics, Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8, Canada

infants to participate in the circumcision trial were asked to enrol their infants in this study and sign a consent form for their participation. We recruited uncircumcised infants from the same study by the same inclusion criteria as for the circumcised infants, the difference being that their parents had chosen not to have their infants circumcised. The protocol received approval from the Research Ethics Boards of the Hospital for Sick Children and Women's College Hospital.

The setting for this study was the clinic of the infant's primary care physician, where vaccination was done. Each infant's physician was contacted before the study commenced and informed about its purpose and procedures. One of the investigators telephoned all the parents 2–4 weeks before the anticipated date of the 4-month or 6-month vaccination to obtain details of the appointment date and time. We chose to study pain response during routine vaccination at 4 or 6 months to reduce the effects of fear and anticipation on infant pain response seen in older infants and children, and because vaccination pain responses do not vary greatly within this age range.<sup>9</sup>

Parents were sent copies of the revised infant temperament questionnaire for infants aged 4–8 months,<sup>12</sup> to complete within

*« Quelle que soit la guérison, il n'y a jamais retour à l'état naïf »*

Georges Canguilhem  
(Le Normal et le pathologique)



# Plan

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2.1. douloureuse

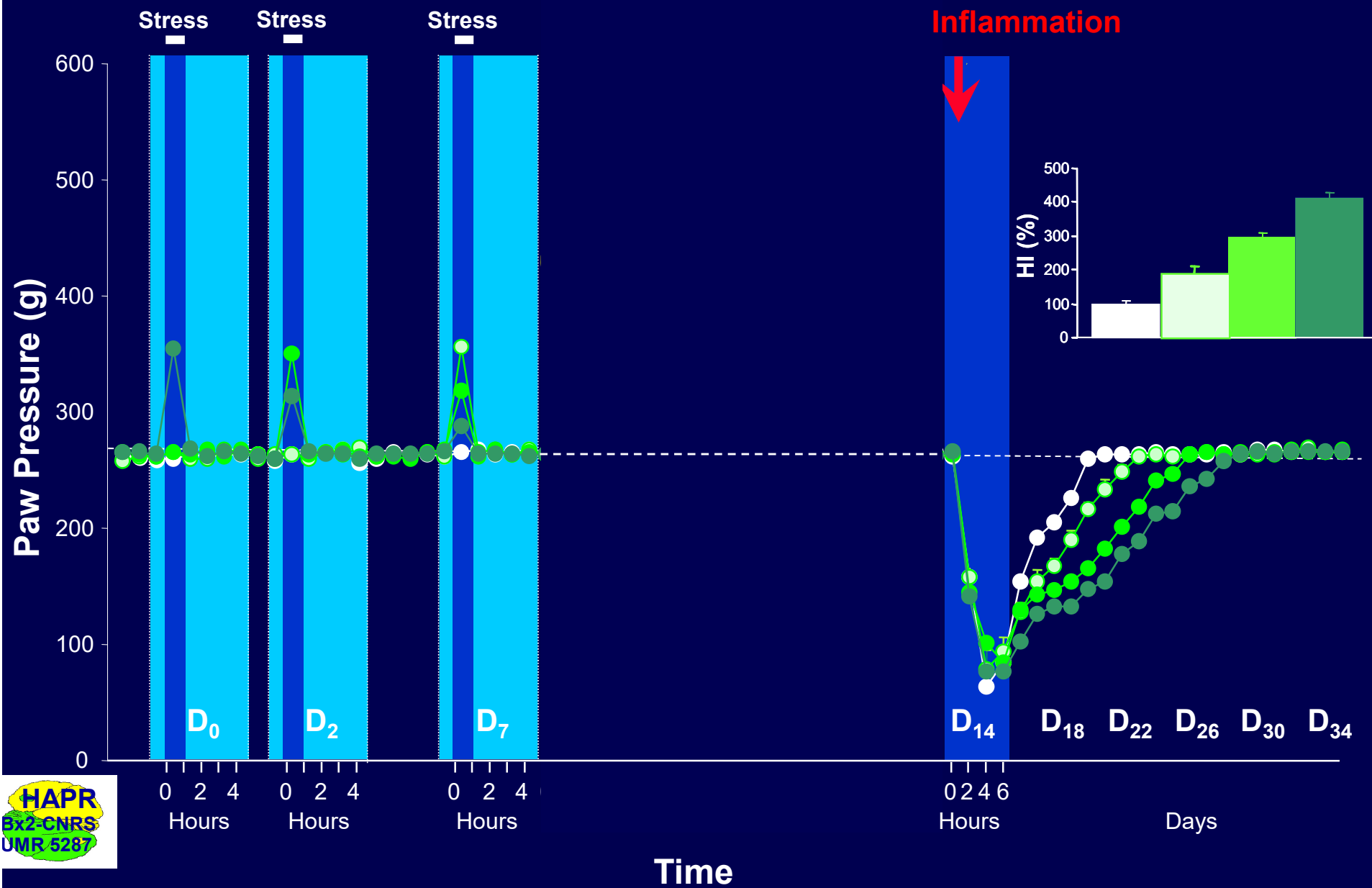
2.2. non douloureuse

2.3. pharmacologique

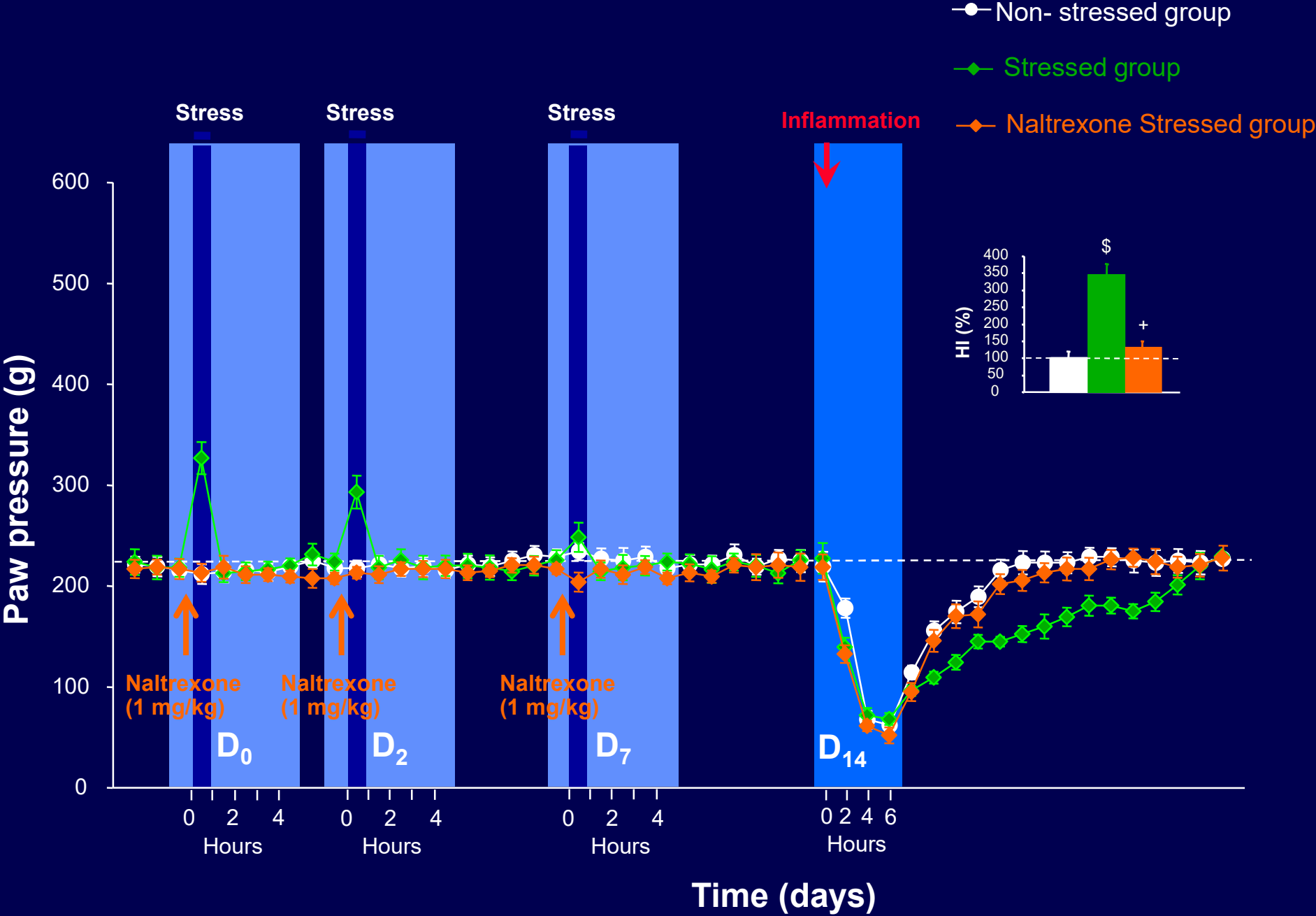
2.4. nutritionnelle

3. Interactions sociales (*compagnonnage*)  
(*pain sickness*)

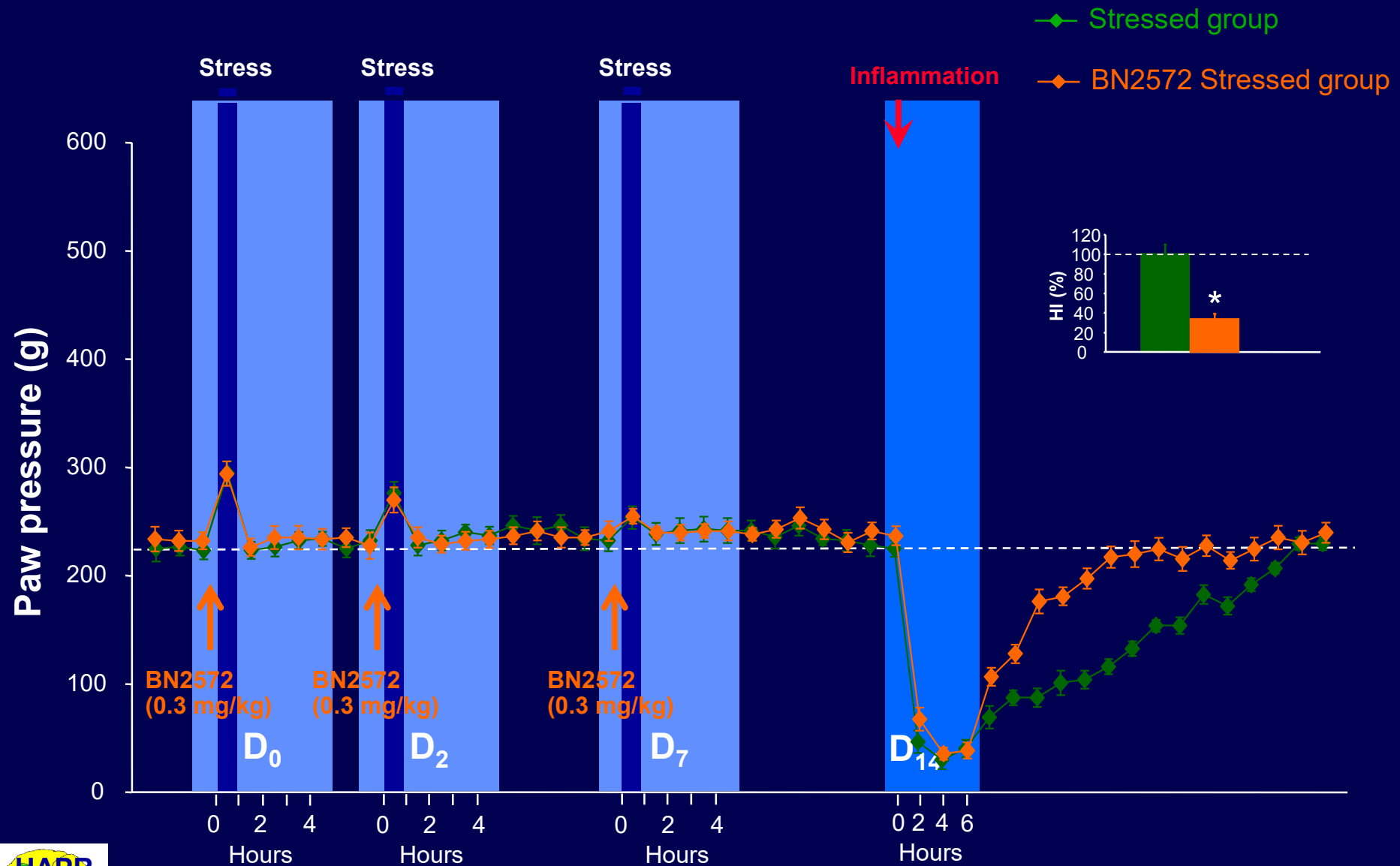
# Dose-réponse stress / Patte ipsilatérale



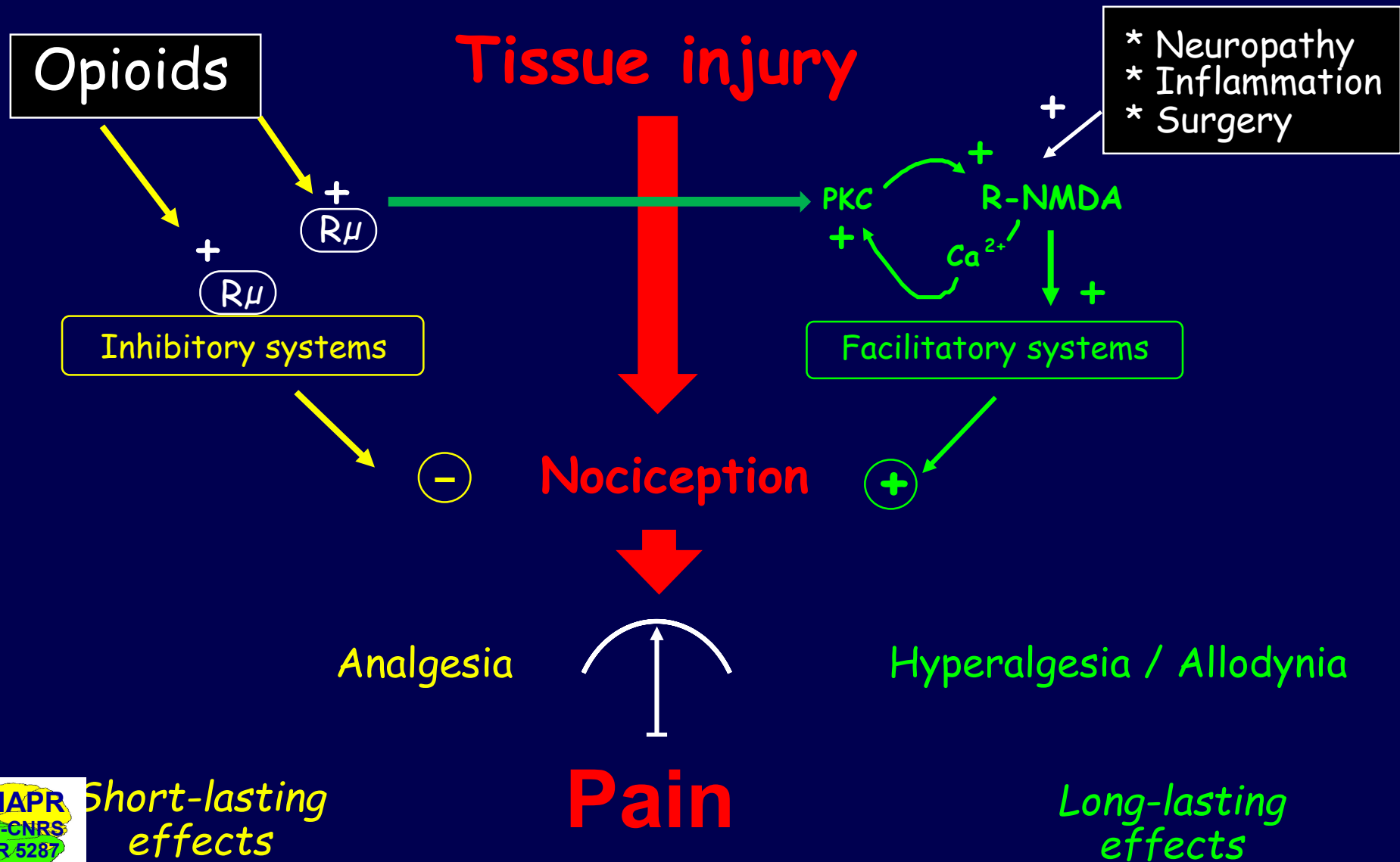
# Paw pressure vocalization test



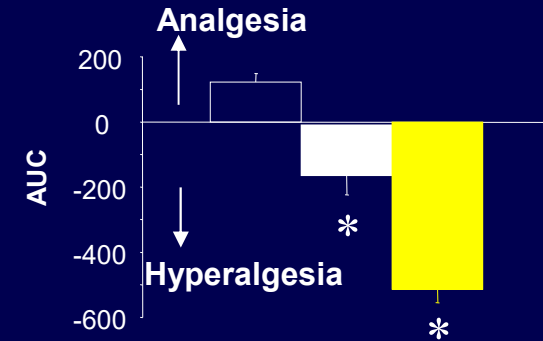
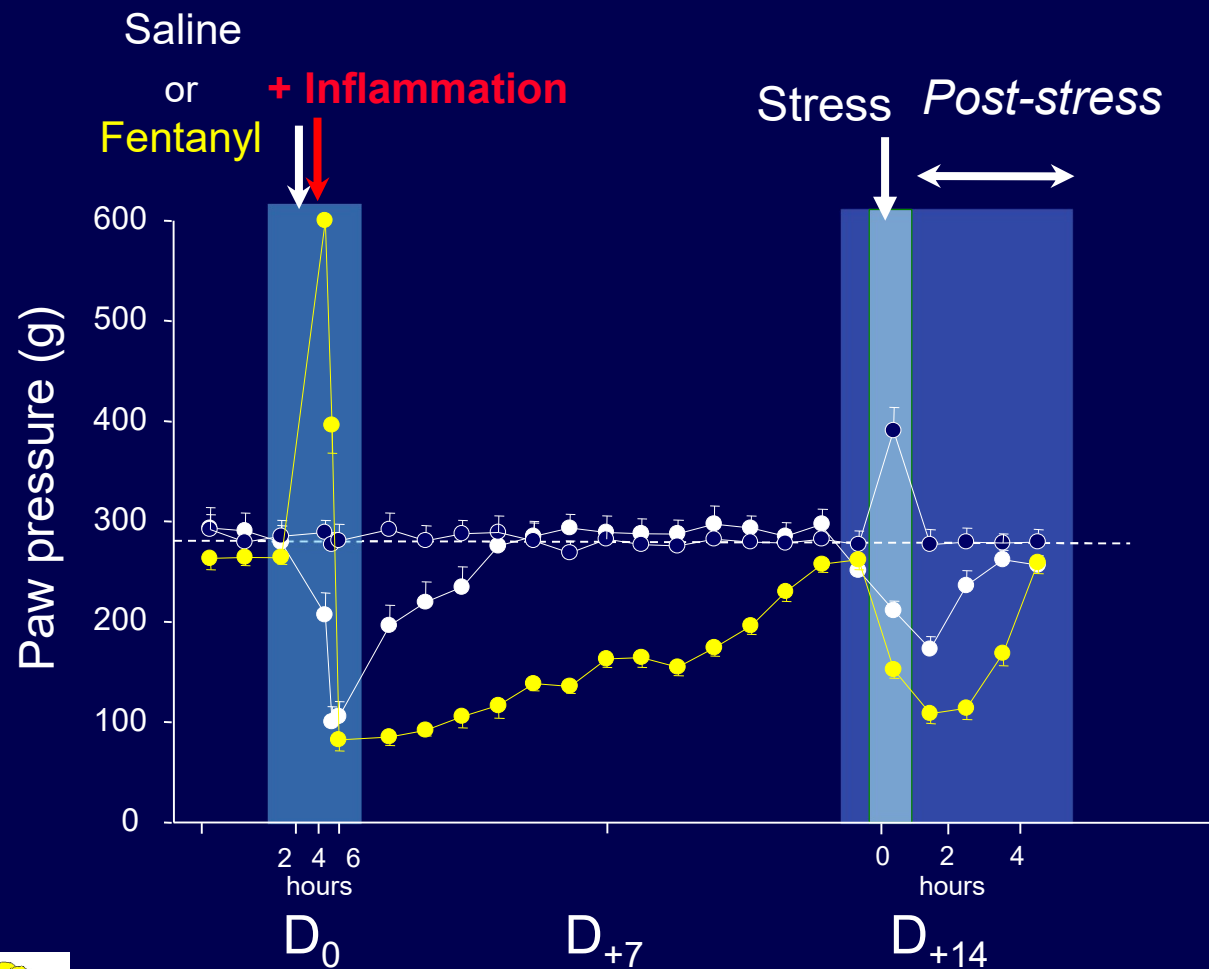
# Paw pressure vocalization test



La douleur: un équilibre entre  **systèmes inhibiteurs**   
et  
 **systèmes facilitateurs**

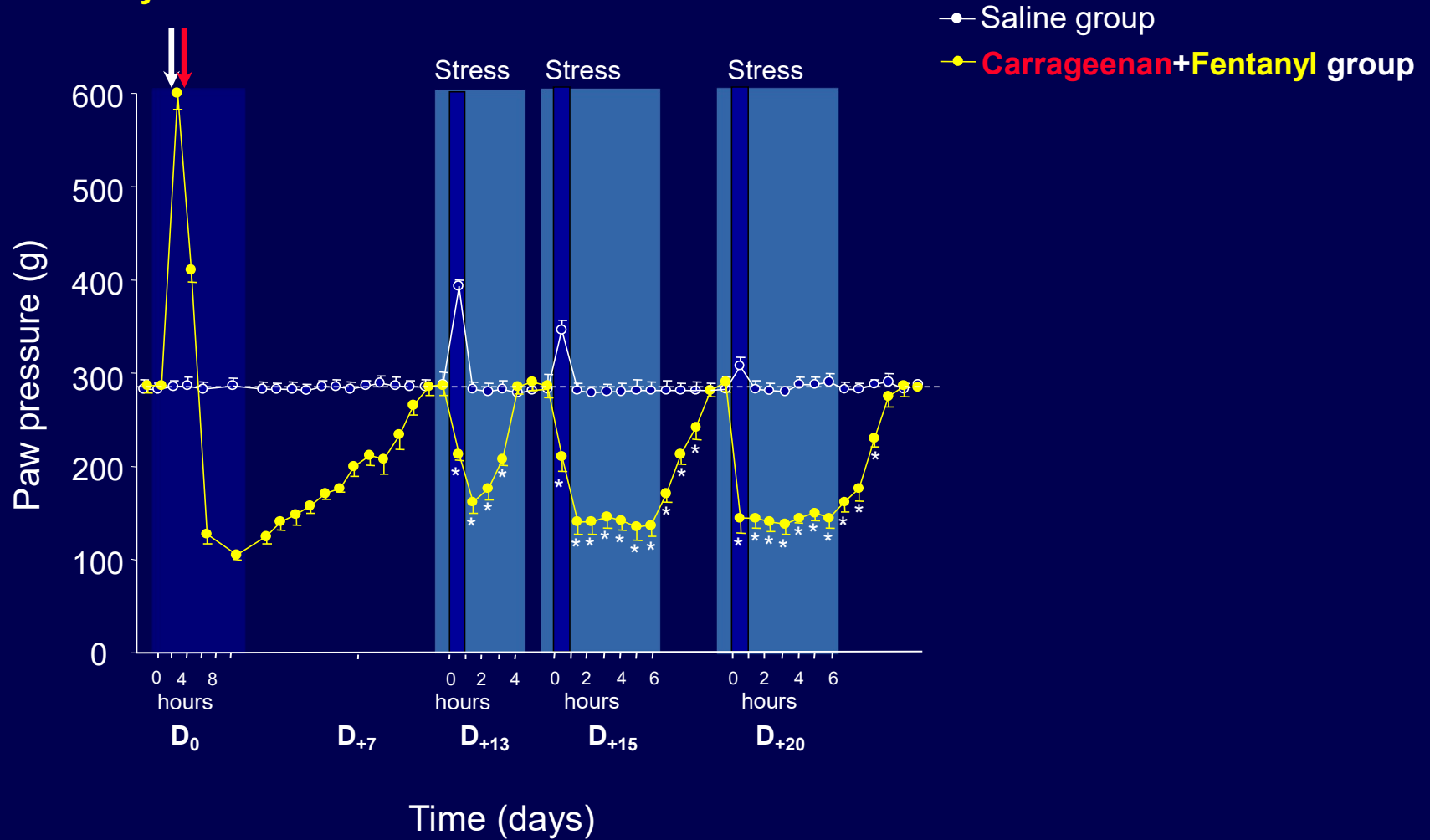


# Stress-induced analgesia or hyperalgesia ?



# Repetitive stress

Fentanyl + Inflammation



**Quid des opioïdes exogènes ?**



## Diapositive 24

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**GS1**

Guy Simonnet; 13/11/2019

# Plan

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2. Histoire individuelle (*pain illness*)

2.1. douloureuse

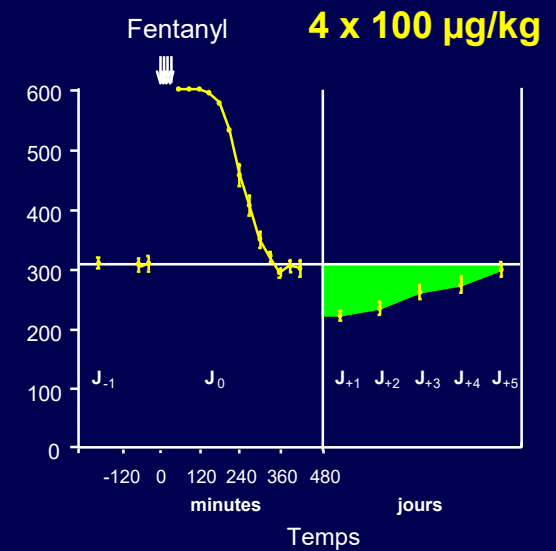
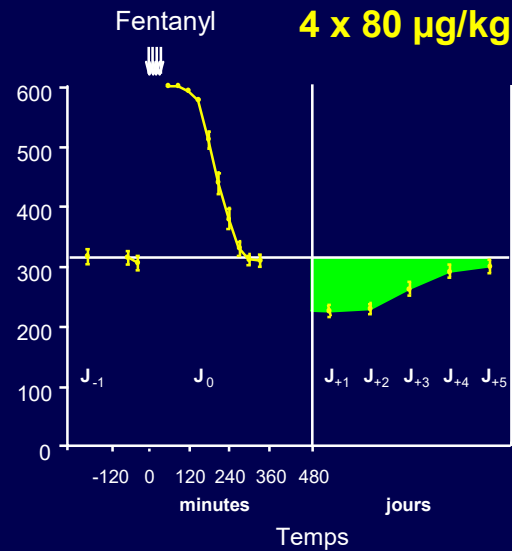
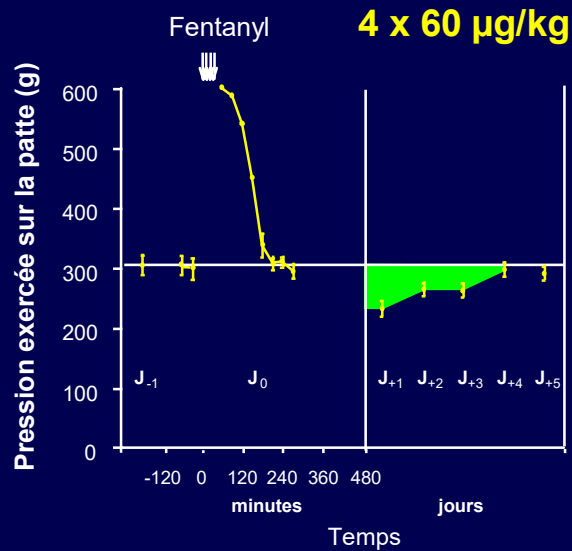
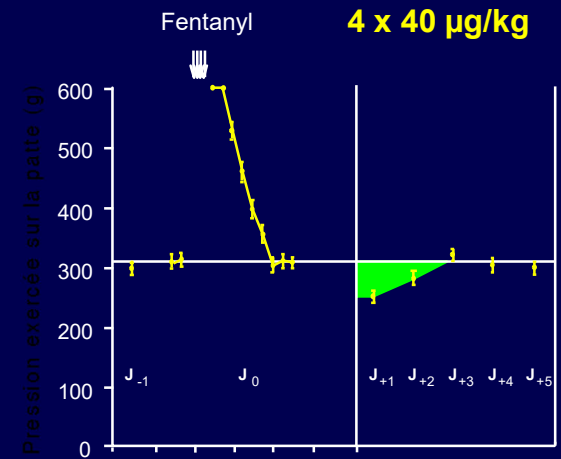
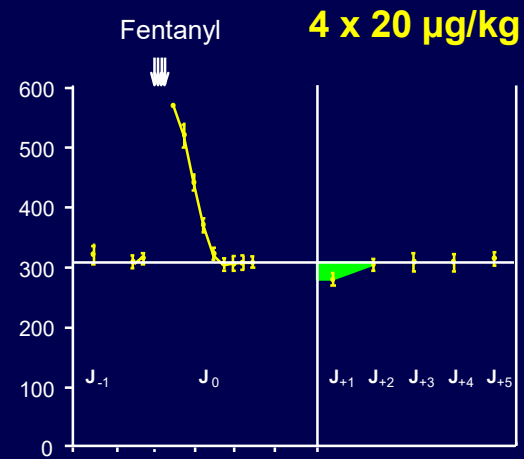
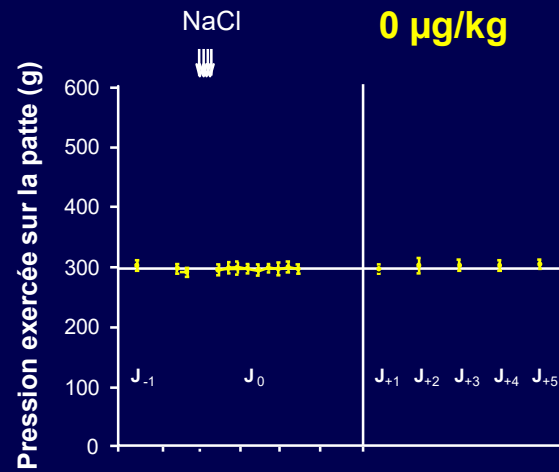
2.2. non douloureuse

2.3. pharmacologique

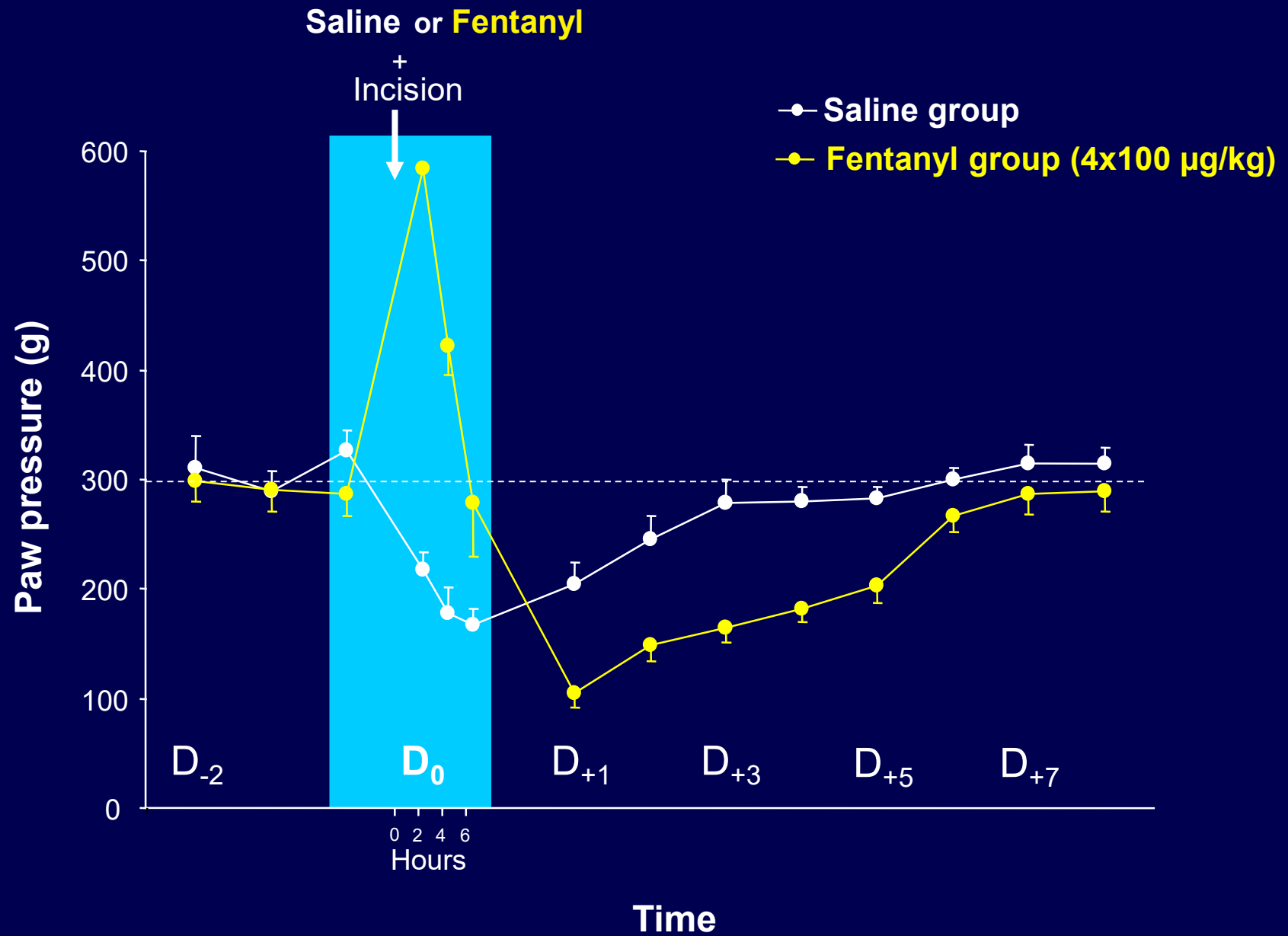
3. Interactions sociales (*compagnonnage*)  
(*pain sickness*)

# Le cas du fentanyl

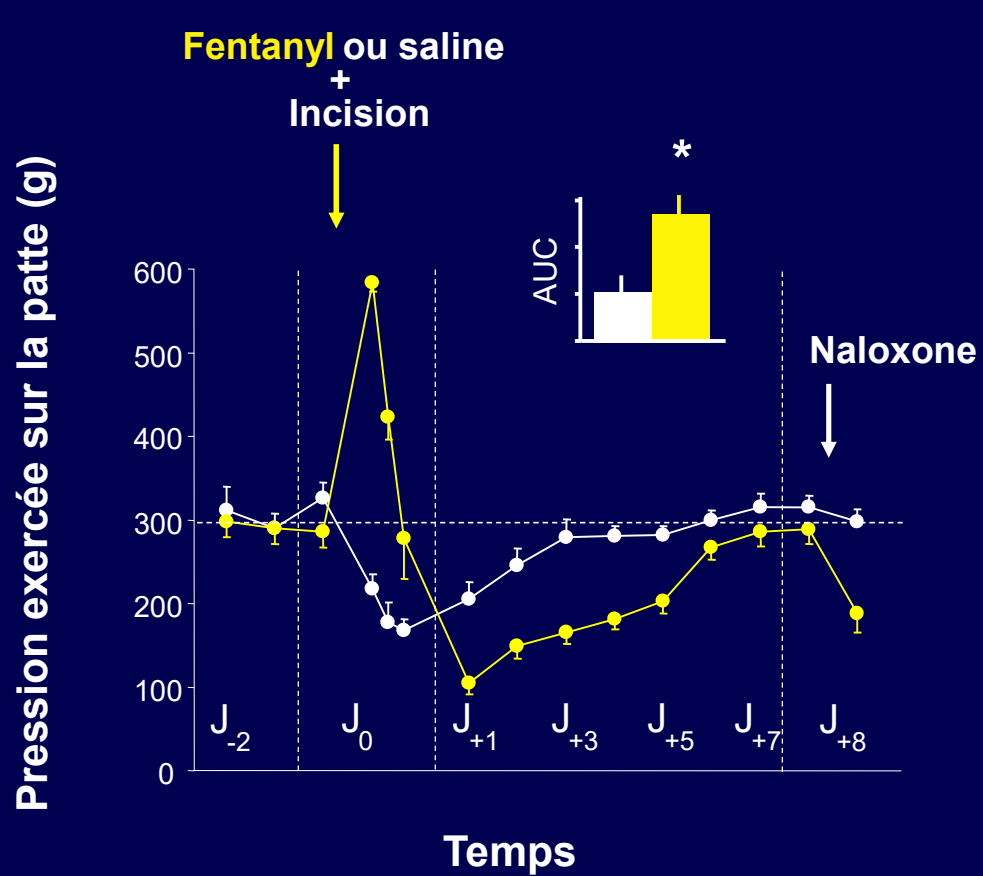
## Effet dose



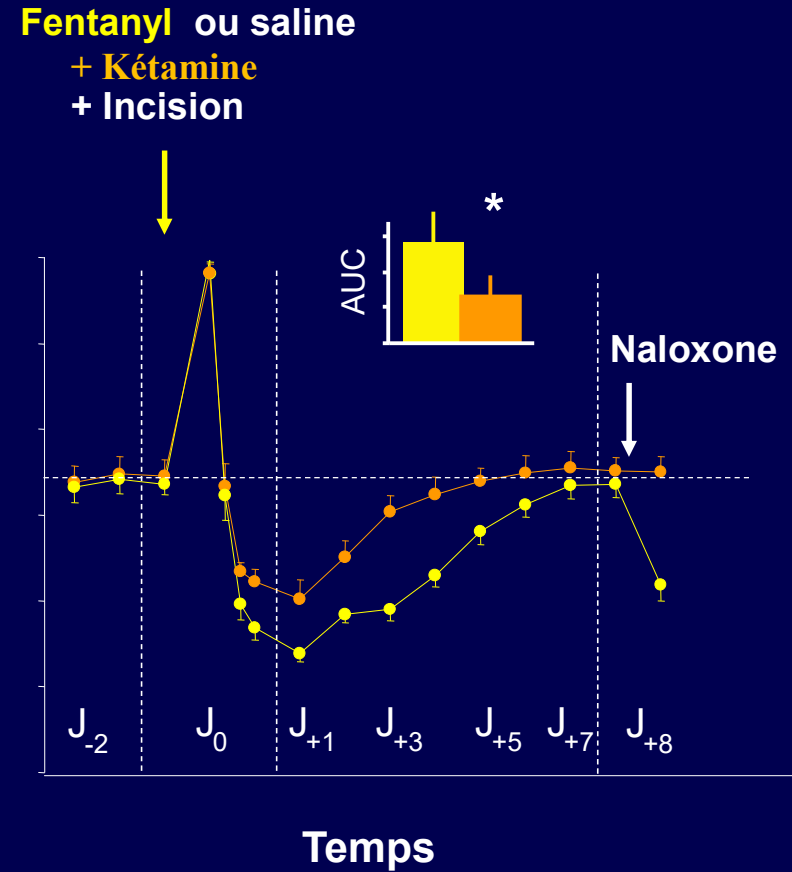
# Incisional pain model



# Test de Randall-Selitto



- Groupe Sérum Salé
- Groupe Fentanyl 4x100µg



- Groupe Fentanyl + Kétamine
- Groupe Fentanyl + Sérum Salé

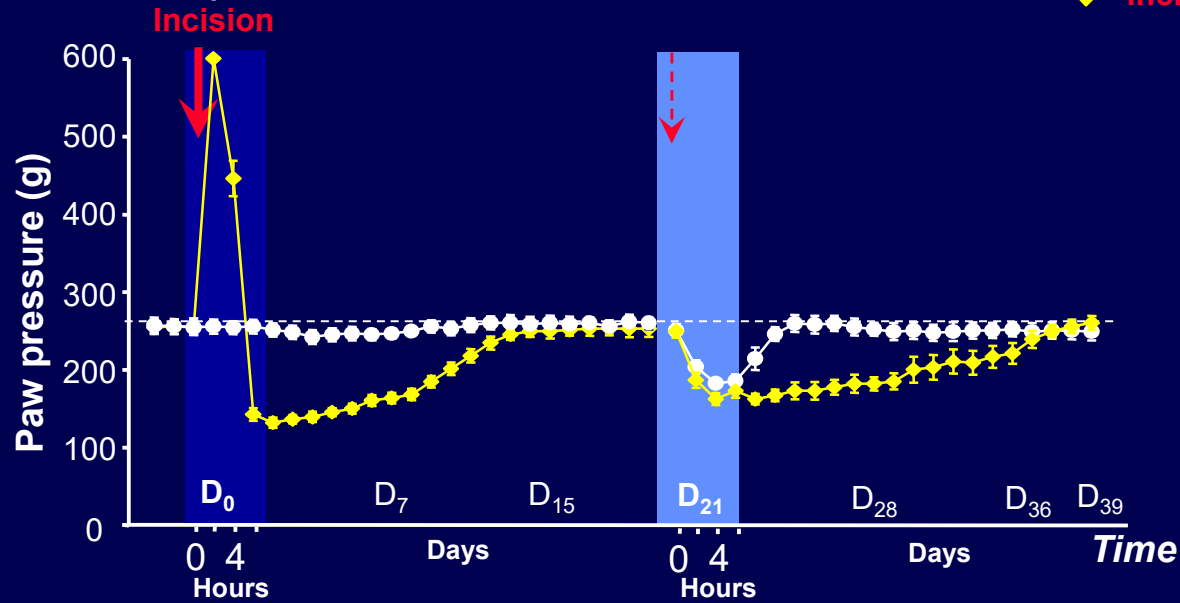
# Paw pressure vocalization test

Saline or Fentanyl (4x100 µg/kg)

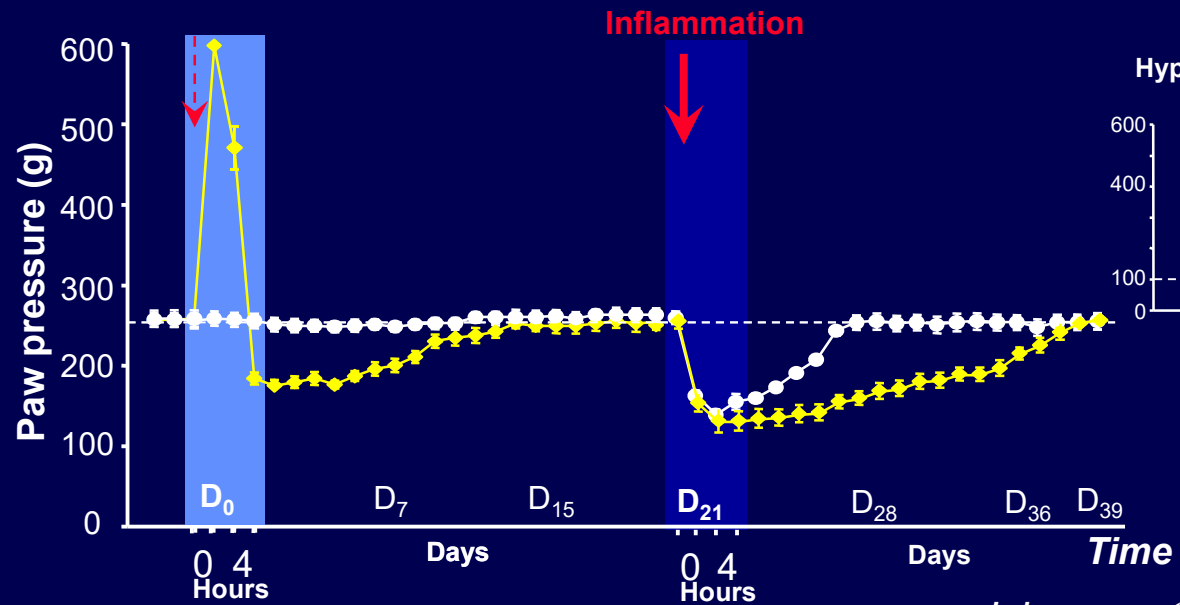
● Control group

◆ Incision / Fentanyl group

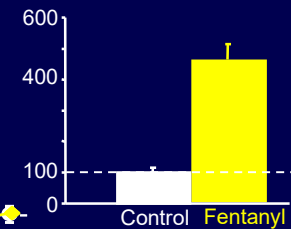
*Patte lésée*



*Patte non lésée*



Hyperalgesic index (%)



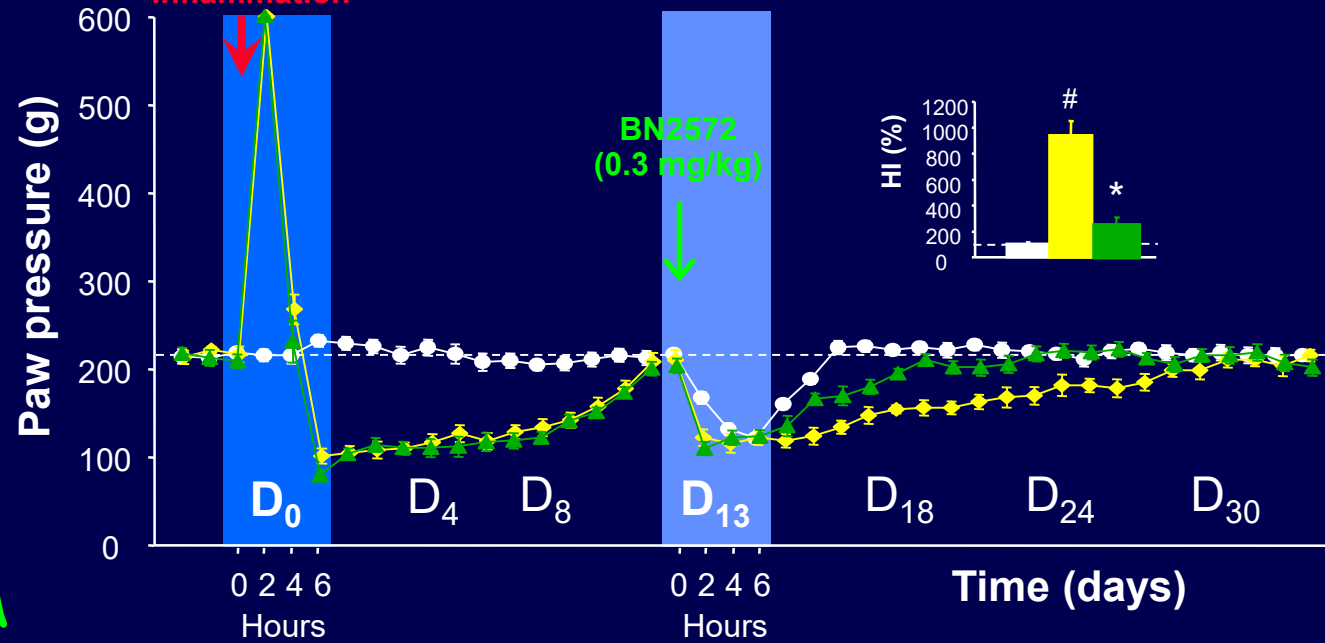
# Paw pressure vocalization test

Fentanyl (4 x 100 µg/kg)

Inflammation

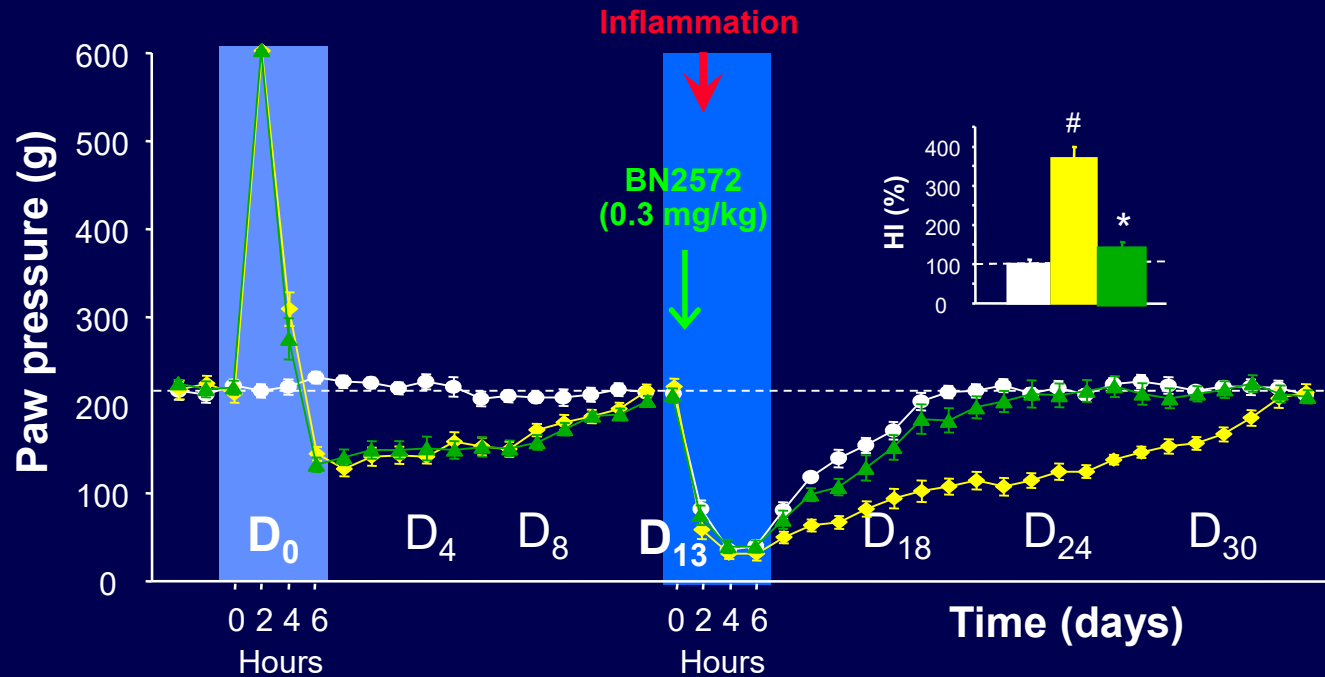
BN2572  
(0.3 mg/kg)

Left hind paw



Anti-NMDA

Right hind paw



Quid de notre sensibilité aux  
antalgiques en fonction de  
notre histoire individuelle ?



## View Through a Window May Influence Recovery from Surgery

*Abstract. Records on recovery after cholecystectomy of patients in a suburban Pennsylvania hospital between 1972 and 1981 were examined to determine whether assignment to a room with a window view of a natural setting might have restorative influences. Twenty-three surgical patients assigned to rooms with windows looking out on a natural scene had shorter postoperative hospital stays, received fewer negative evaluative comments in nurses' notes, and took fewer potent analgesics than 23 matched patients in similar rooms with windows facing a brick building wall.*

Table 1. Comparison of analgesic doses per patient for wall-view and tree-view groups.

Analgesic strength	Number of doses					
	Days 0-1		Days 2-5		Days 6-7	
	Wall group	Tree group	Wall group	Tree group	Wall group	Tree group
Strong	2.56	2.40	2.48	0.96	0.22	0.17
Moderate	4.00	5.00	3.65	1.74	0.35	0.17
Weak	0.23	0.30	2.57	5.39	0.96	1.09

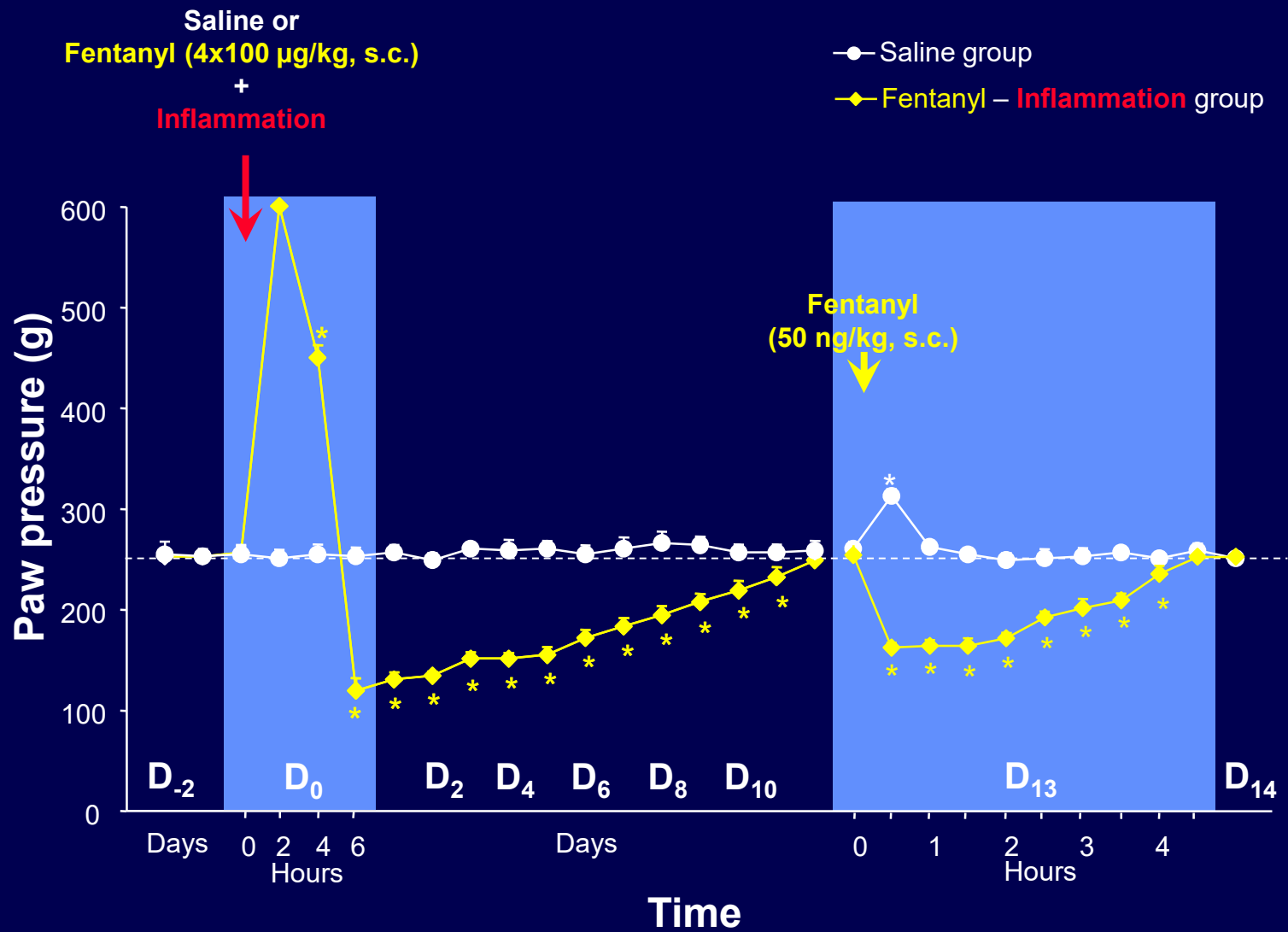
420

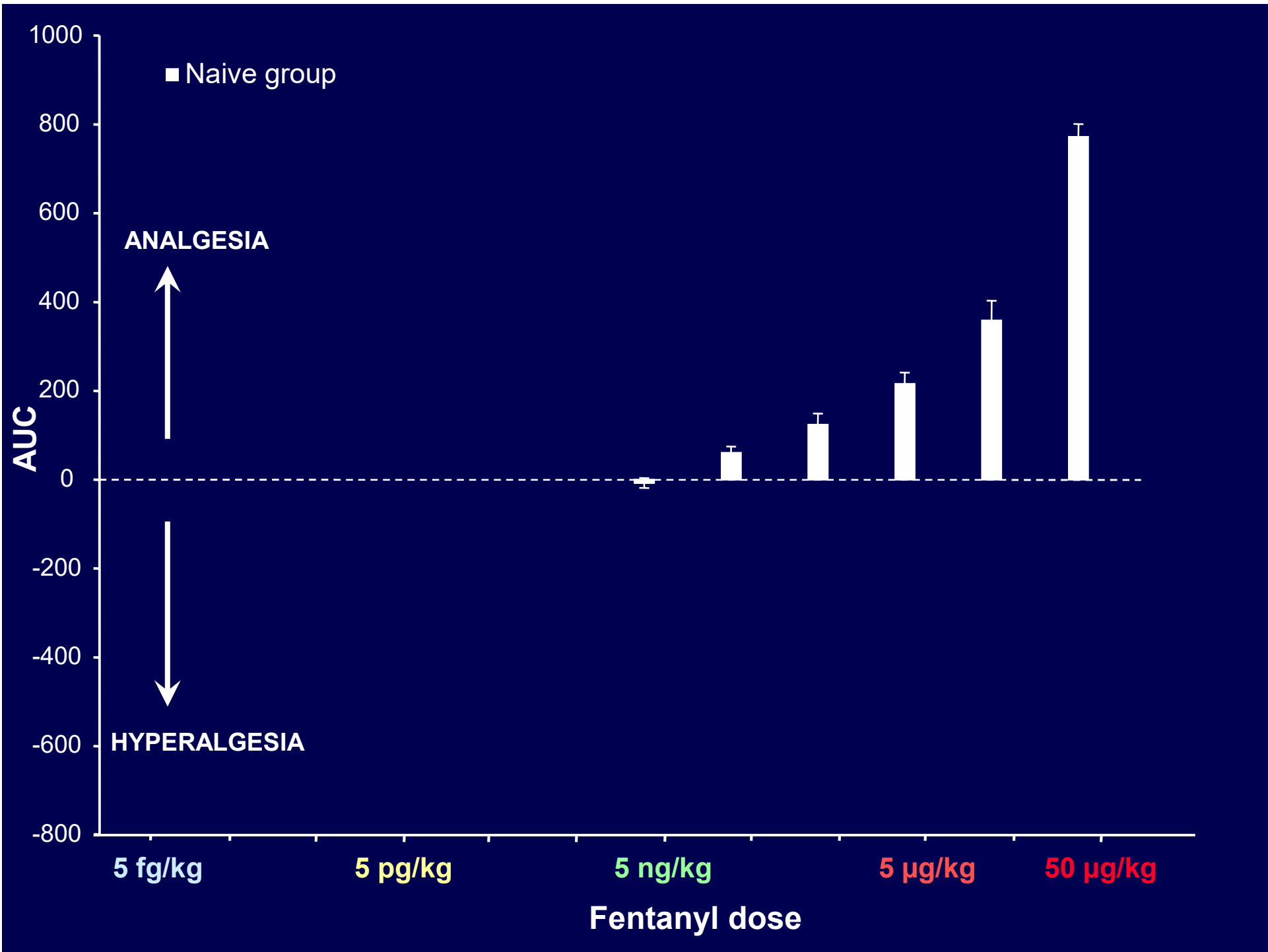
ROGER S. ULRICH

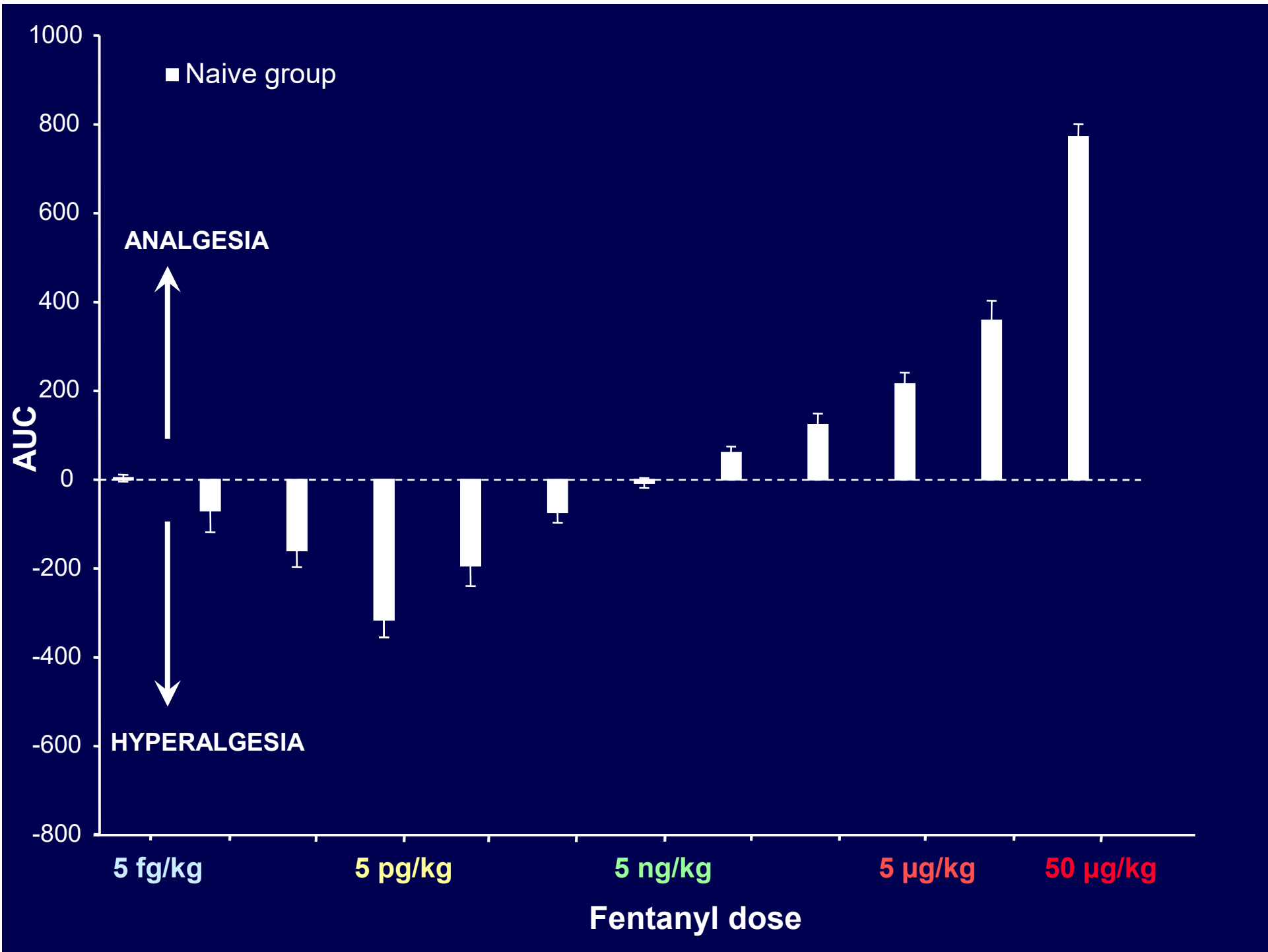
*Department of Geography,  
University of Delaware, Newark 19716*

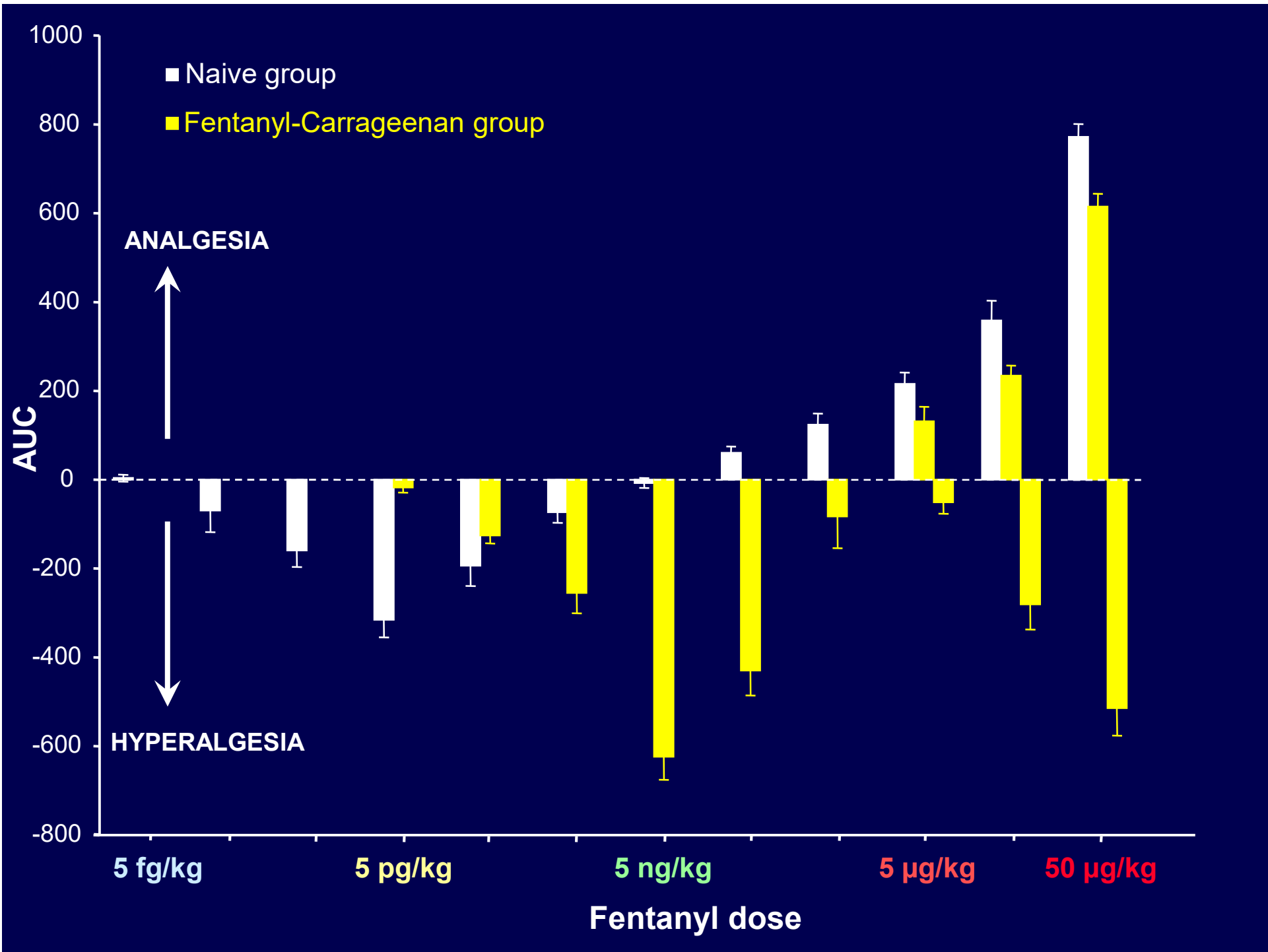
SCIENCE, VOL. 224 27 APRIL 1984

# Fentanyl ultra-low dose









L'hypersensibilité à long terme facilitée  
par les analgésiques opioïdes  
doit-elle nous inciter à supprimer  
l'usage des substances opioïdes ?



**NON!**



# Plan

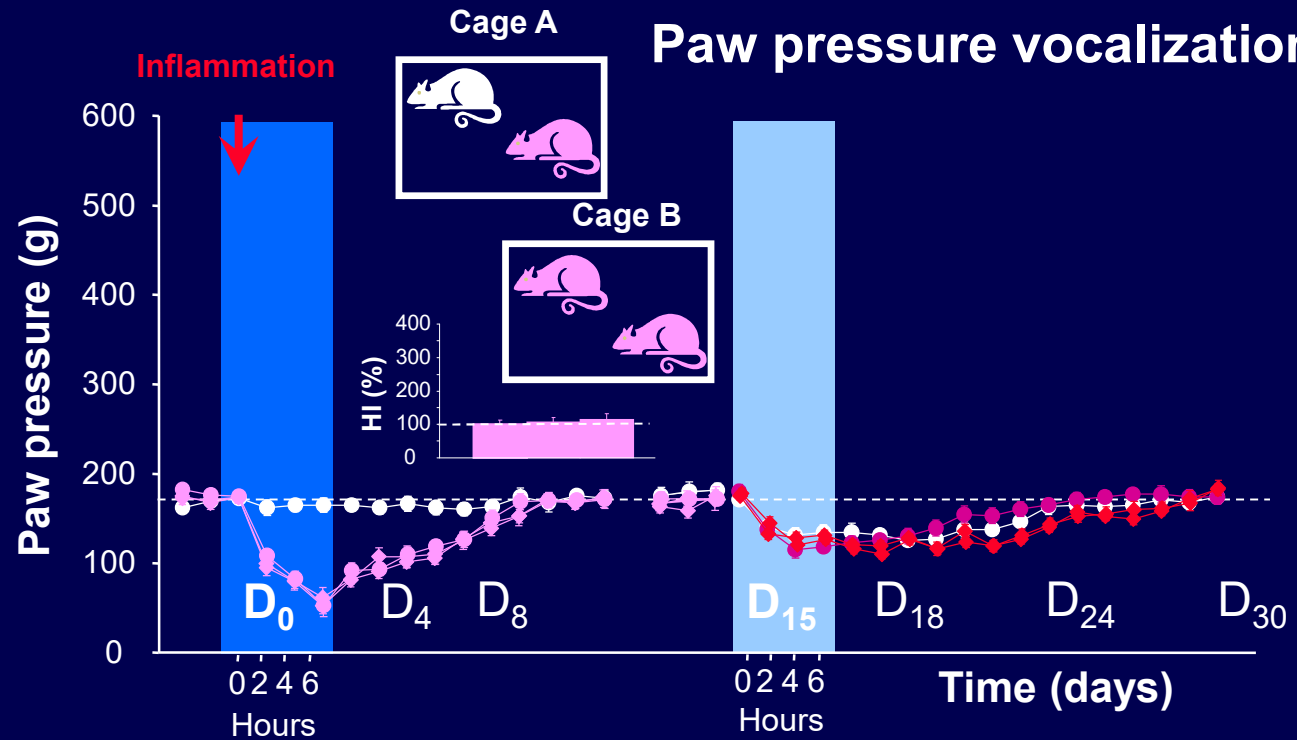
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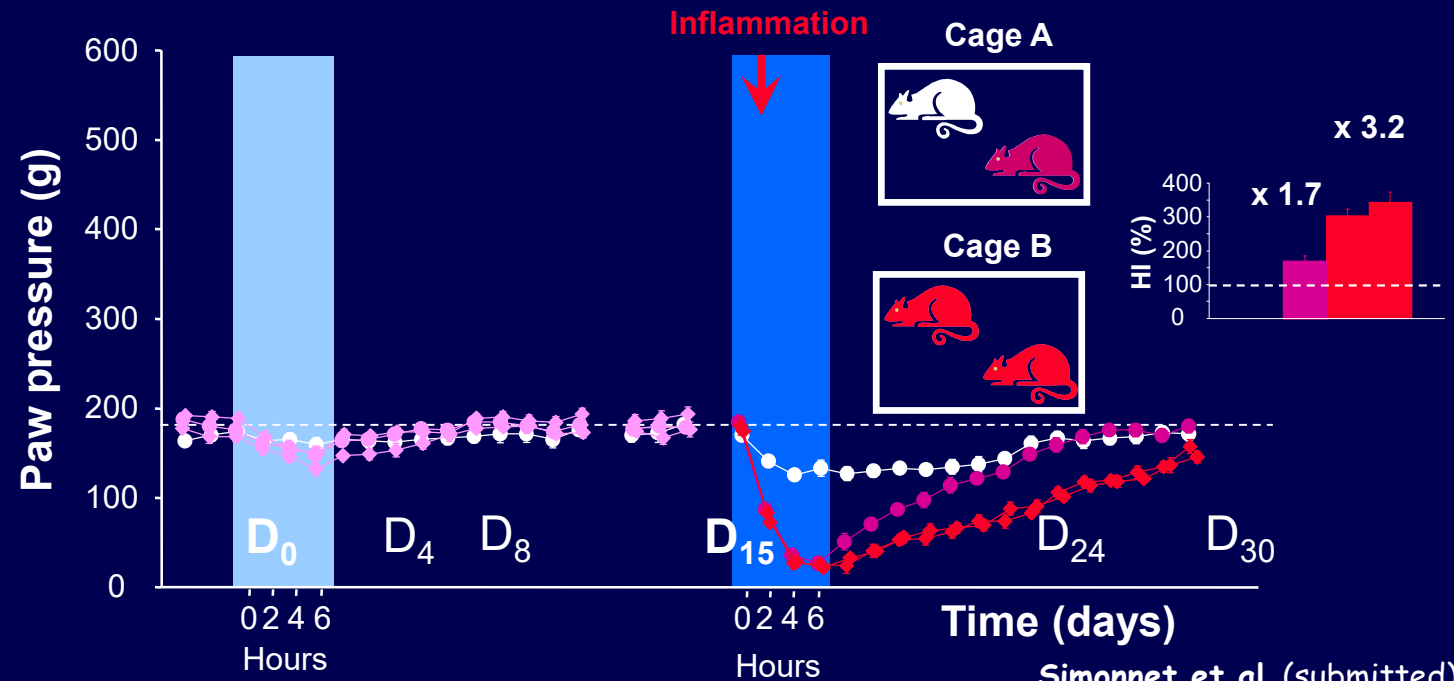


# Paw pressure vocalization test

Left hind paw

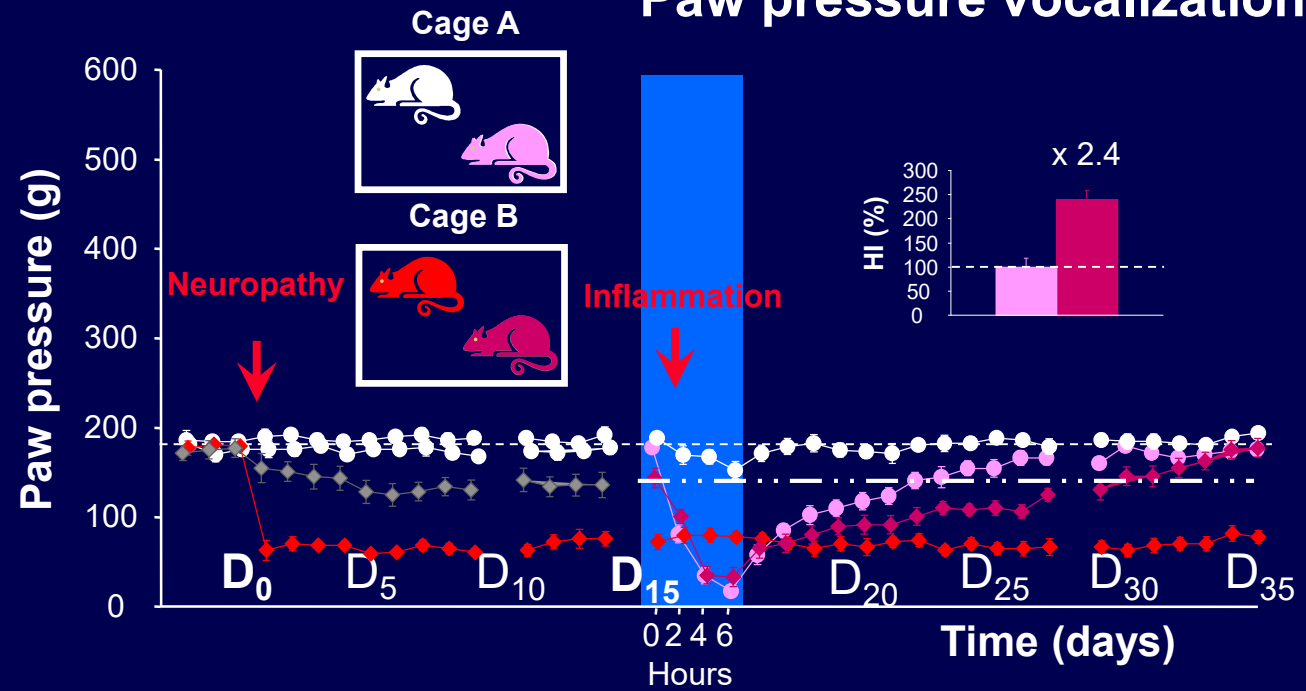


Right hind paw

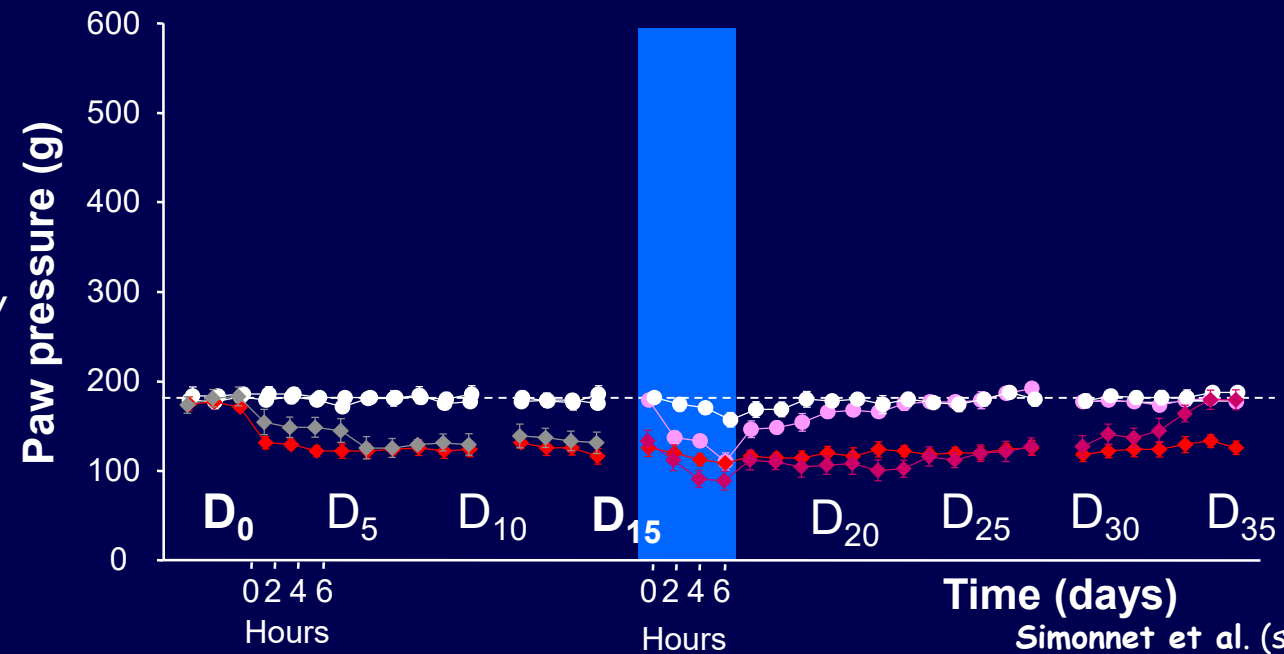


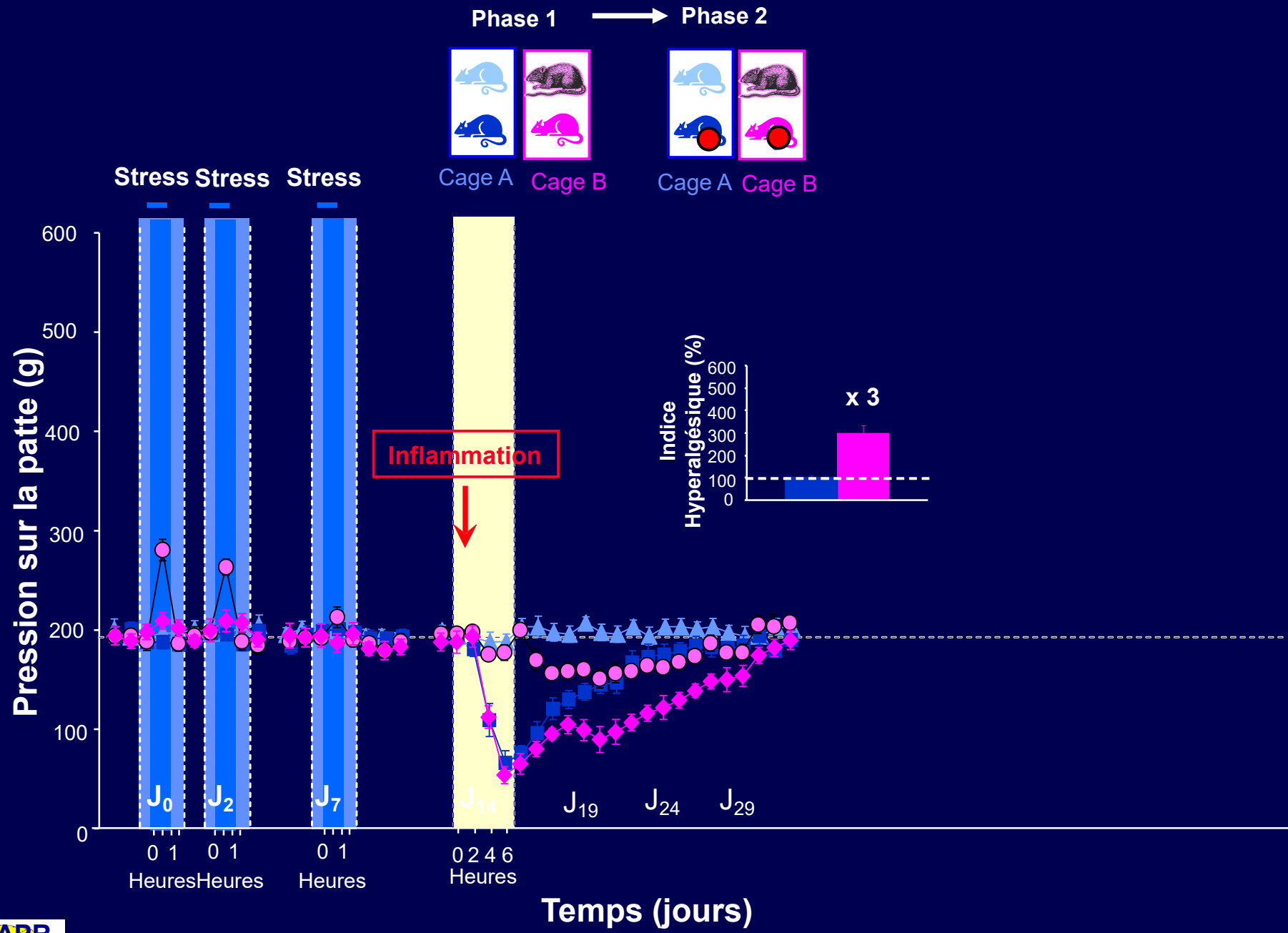
# Paw pressure vocalization test

*Injured hind paw*



*Non-injured hind paw*





# Qui doit-on soigner ?

Le patient, le « conjoint », le groupe social ?

*(une organisation sociale « délétère » ??????)*

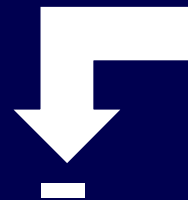
# Vers de nouvelles stratégies thérapeutiques ?

# De la douleur aiguë aux douleurs exagérées

**Lésion tissulaire**



**Douleur aiguë**



**Antalgiques classiques (3 paliers OMS)**

**Processus nociceptifs**



**Douleurs chroniques  
Douleurs aiguës  
exagérées**

**Processus de sensibilisation**

**+**



**-**



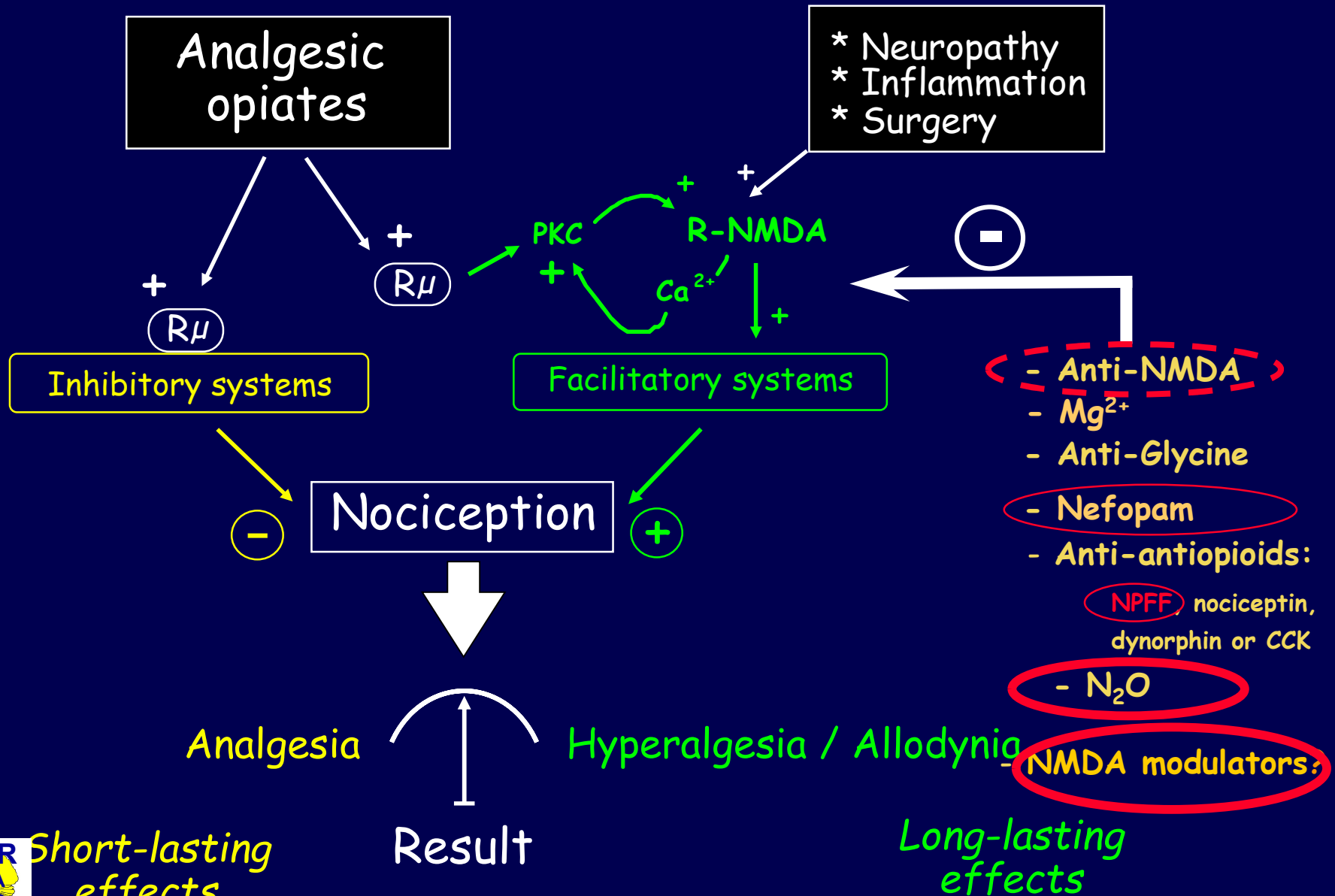
**Agents anti-sensibilisants  
(Stratégies anti-hyperalgésiques)**

Histoire de l'individu :

Douleurs, stress, interactions sociales,  
nutrition, prise d'opioïdes, tryptans...

Patrimoine génétique

# Pharmacological proposals



*« Plutôt guérir de sa douleur, que guérir sa douleur »*

Anne-Françoise Allaz  
(Le messenger boiteux)



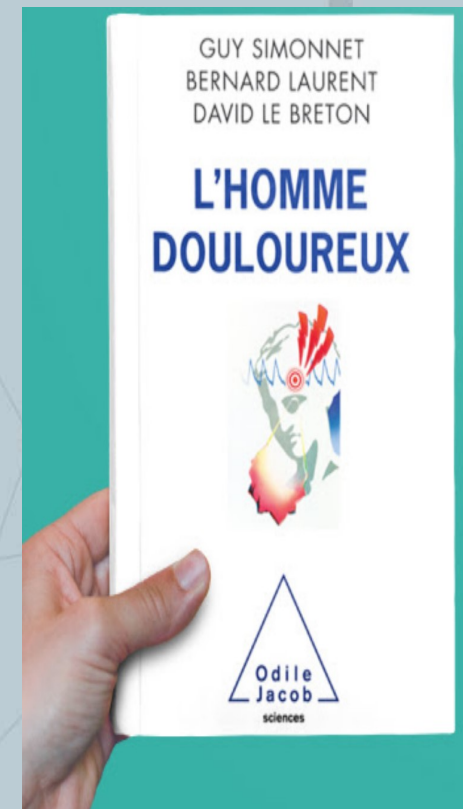
# DOULEUR

## 3° Modèle constructionniste

### Contexte préexistant

- *Expériences*
- *Vécu douloureux*

La douleur ne s'élabore pas au sein d'un cerveau amnésique, mais au sein d'un système nerveux façonné par le passé singulier et les expériences de chacun.



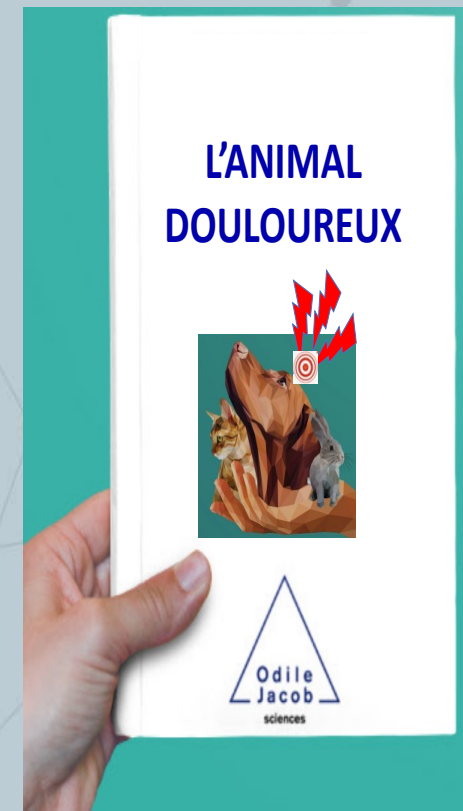
# DOULEUR

## 3° Modèle constructionniste

### Contexte préexistant

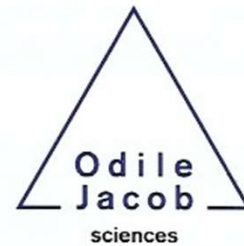
- *Expériences*
- *Vécu douloureux*

La douleur ne s'élabore pas au sein d'un cerveau amnésique, mais au sein d'un système nerveux façonné par le passé singulier et les expériences de chacun.



GUY SIMONNET  
BERNARD LAURENT  
DAVID LE BRETON

# L'HOMME DOULOUREUX

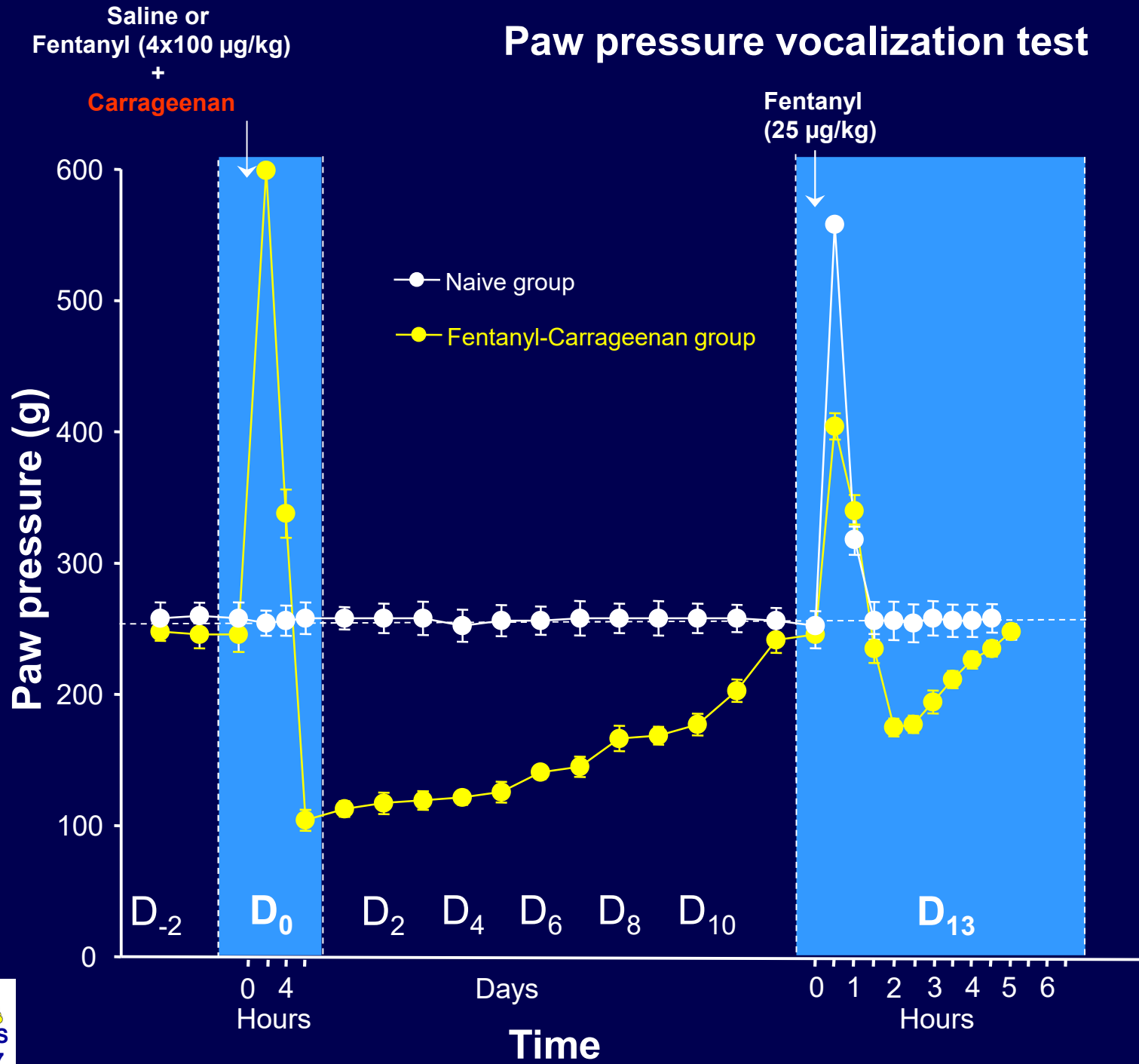


[ga.simonnet@gmail.com](mailto:ga.simonnet@gmail.com)





# Paw pressure vocalization test



## Are Psychological Predictors of Chronic Postsurgical Pain Dependent on the Surgical Model? A Comparison of Total Knee Arthroplasty and Breast Surgery for Cancer

Anne Masselin-Dubois,<sup>\*,†</sup> Nadine Attal,<sup>\*,†,‡</sup> Dominique Fletcher,<sup>\*,†,‡,§</sup> Christian Jayr,<sup>¶</sup> Aline Albi,<sup>¶</sup> Jacques Fermanian,<sup>||</sup> Didier Bouhassira,<sup>\*,†,‡</sup> and Sophie Baudic<sup>\*,†,‡</sup>

<sup>\*</sup>INSERM U-987, Boulogne-Billancourt, France.

<sup>†</sup>CHU Ambroise Paré, GH Paris Ile de France Ouest, APHP, Boulogne-Billancourt, France.

<sup>‡</sup>Université Versailles-Saint-Quentin, Versailles, France.

<sup>§</sup>Service d'anesthésie-réanimation chirurgicale, CHU Raymond Poincaré, GH Paris Ile de France Ouest, APHP, Garches, France.

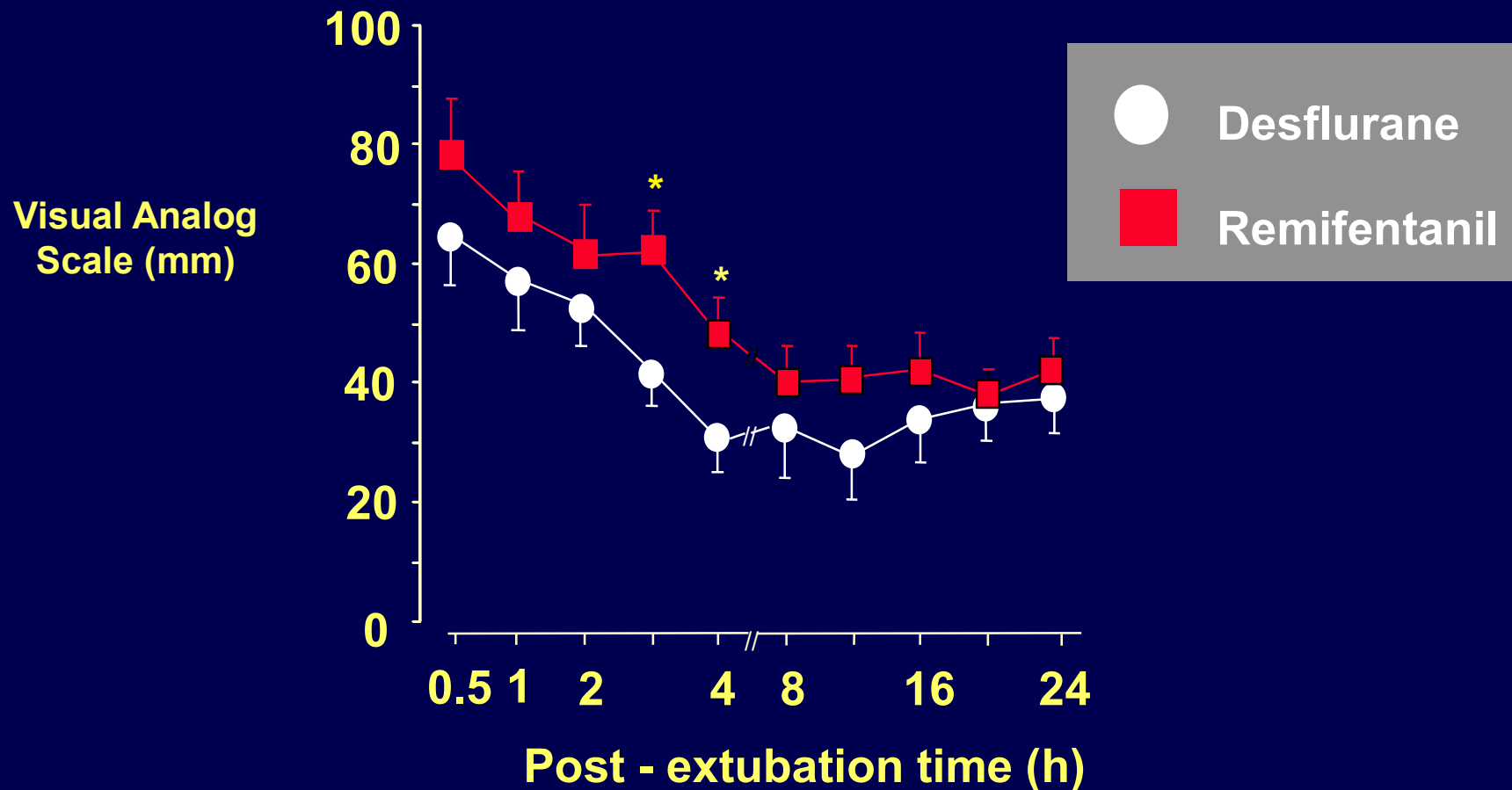
<sup>¶</sup>Service de chirurgie générale, Hôpital René Huguenin-Institut Curie, Saint Cloud, France.

<sup>||</sup>Service de biostatistiques, CHU Necker, APHP, Paris, France.

**Abstract:** Anxiety, depression, and catastrophizing are generally considered to be predictive of chronic postoperative pain, but this may not be the case after all types of surgery, raising the possibility that the results depend on the surgical model. We assessed the predictive value of these factors for chronic postsurgical pain in 2 different surgical models: total knee arthroplasty for osteoarthritis (89 patients, 65% women, age = 69 ± 9 years, baseline pain intensity = 4.7 ± 2.1) and breast surgery for cancer (100 patients, 100% women, age = 55 ± 12 years, no preoperative pain). Data were collected before surgery, then 2 days and 3 months after surgery. Anxiety, depression, and catastrophizing were measured with the Spielberger State-Trait Anxiety Inventory, Beck Depression Inventory, and Pain Catastrophizing Scale, respectively. Pain was assessed with the Brief Pain Inventory. Neuropathic pain was detected with the DN4 questionnaire. Multivariate logistic regression analyses for the total knee arthroplasty and breast surgery models considered together indicated that the presence of clinically meaningful chronic pain at 3 months (pain intensity  $\geq 3/10$ ) was predicted independently by age ( $P = .04$ ), pain intensity on day 2 ( $P = .009$ ), and state anxiety ( $P = .001$ ). Linear regression models also showed that pain magnification, one of the dimensions of catastrophizing, independently predicted chronic pain intensity ( $P = .04$ ). These results were not affected by the surgical model or by the neuropathic characteristics of the pain. Thus, state anxiety and pain magnification seem to constitute psychological risk factors for chronic postsurgical pain relevant in all surgical models.

**Perspective:** This prospective study performed in patients with total knee arthroplasty or breast surgery for cancer shows that state anxiety, amplification of pain, and acute postoperative pain independently predict postsurgical pain at 3 months and that this does not depend on the surgical model.

# Visual analog scale pain scores (0-100 mm) in the two groups during the 24 hours after tracheal extubation

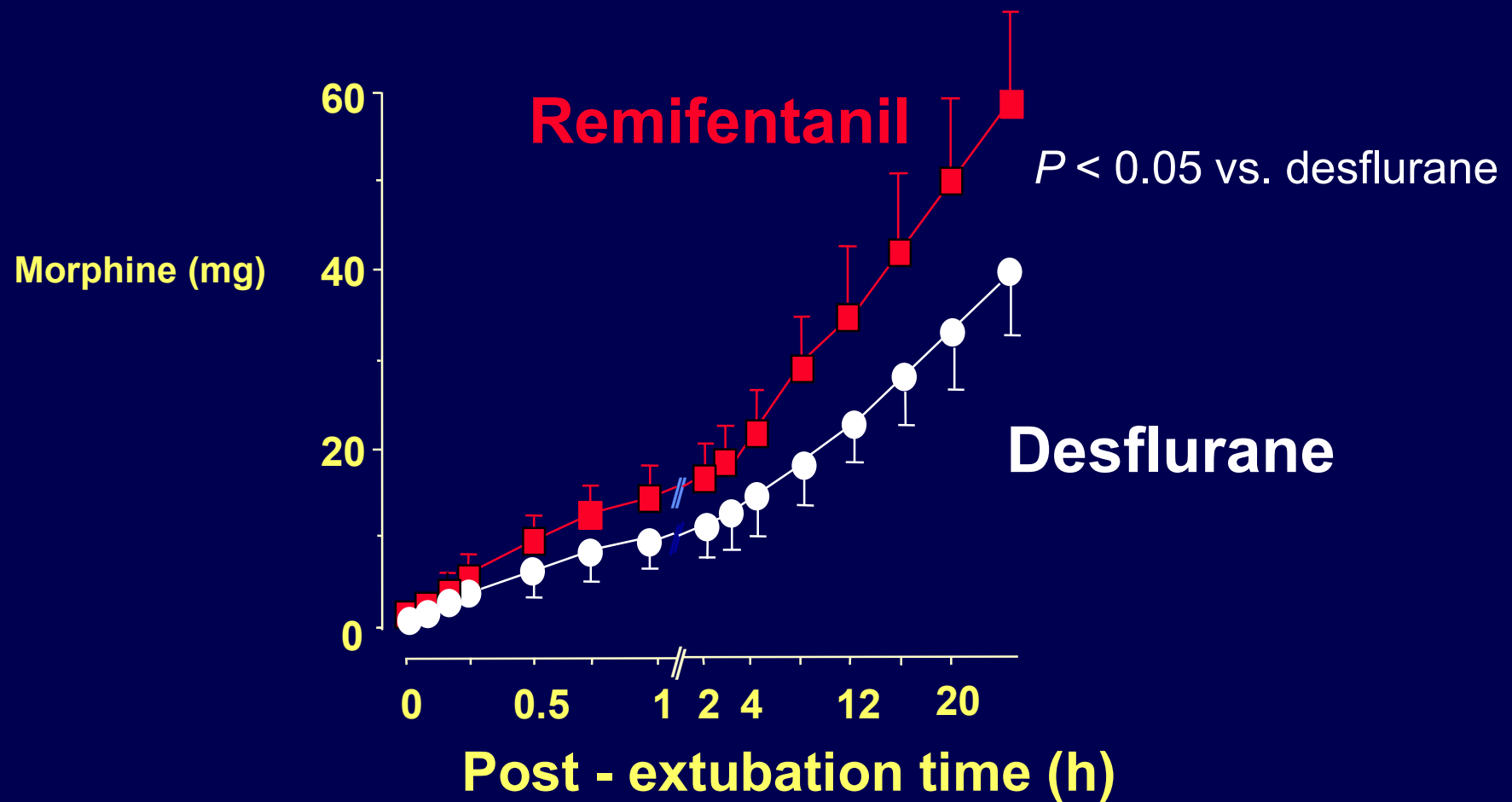


(mean  $\pm$  95% confidence interval)

\*:  $P < 0.05$  vs desflurane



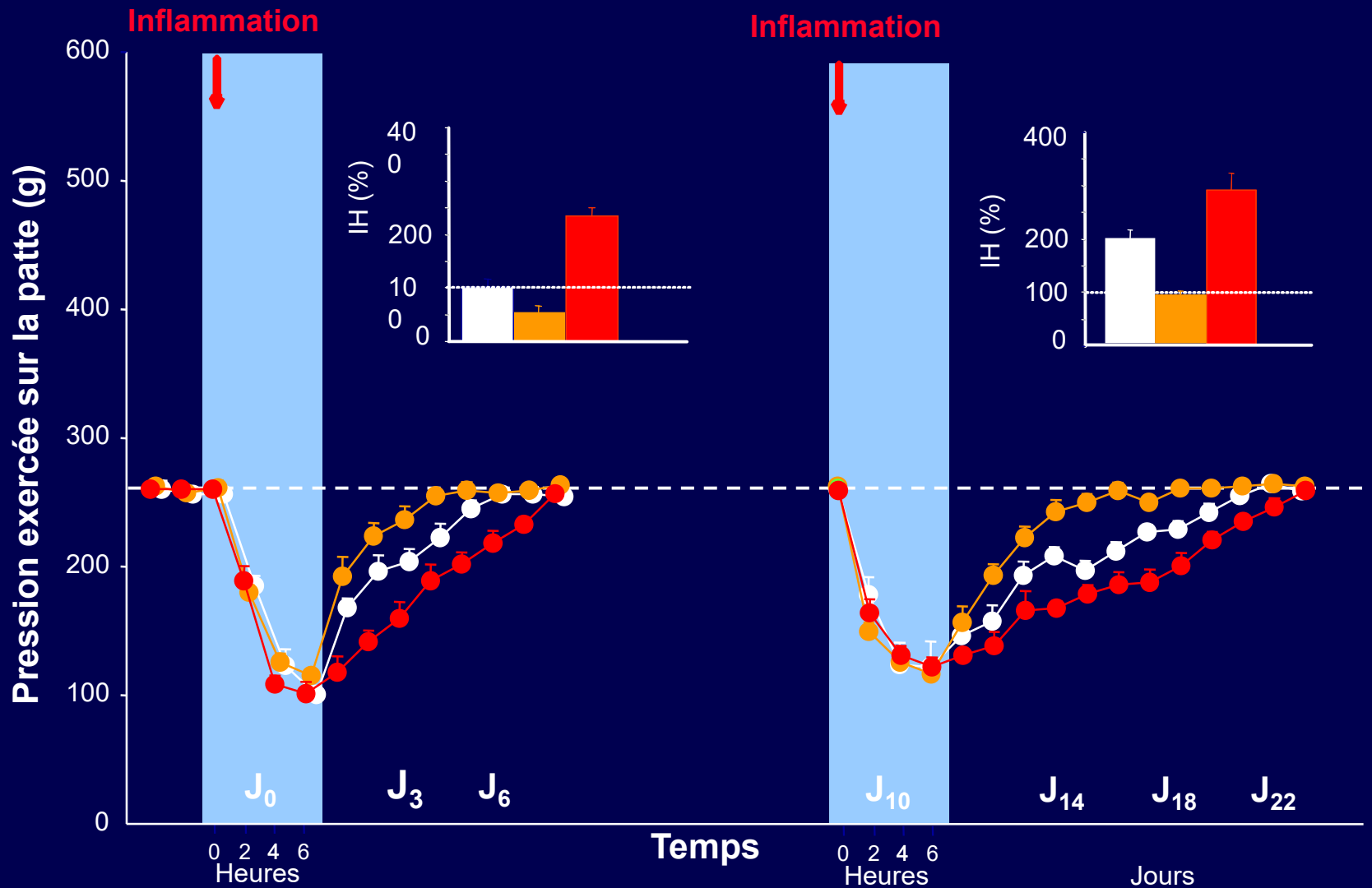
# Remifentanil vs. desflurane based anesthesia

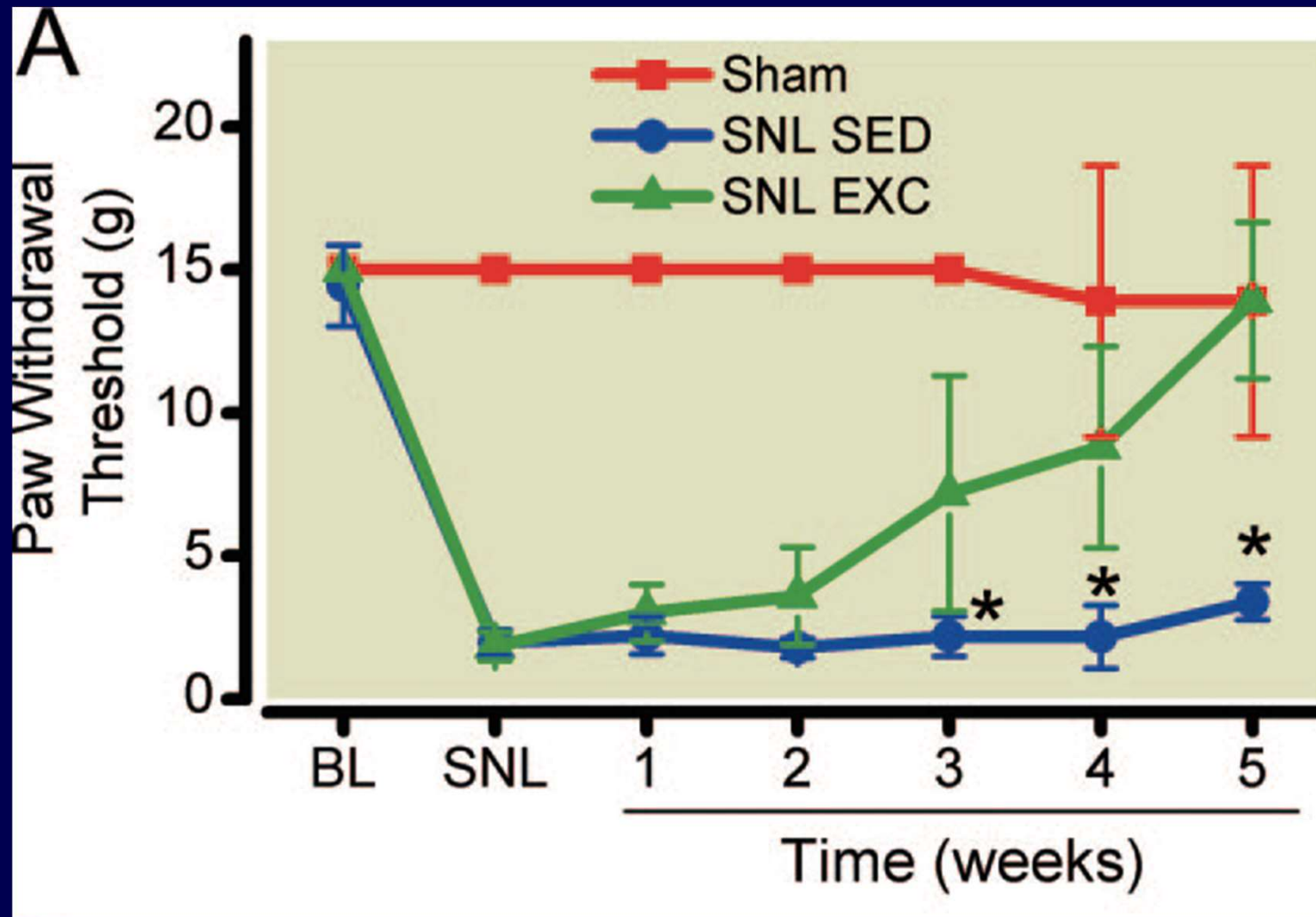


m  $\pm$  95% confidence interval

Guignard et al. Anesthesiology 2000; 93:409-17

# Polyamine levels and pain sensitivity





Regular Exercise Reverses Sensory Hypersensitivity in a Rat Neuropathic Pain Model - Role of Endogenous Opioids

Nicola J. Stagg, et al. *Anesthesiology* 2011; 114:940 - 8.

## *Nitrous Oxide Revisited*

### *Evidence for Potent Antihyperalgesic Properties*

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## Nitrous oxide (N<sub>2</sub>O) prevents latent pain sensitization and long-term anxiety-like behavior in pain and opioid-experienced rats<sup>☆</sup>

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CAPdoulleur  
CHANGE ANIMAL PAIN

1<sup>ère</sup> JOURNÉE DOULEUR  
Boehringer-Ingelheim Bat. Boréal

La Confluence des douleurs  
de l'homme à l'animal :  
l'intelligence des regards croisés  
la rencontre scientifique  
la volonté de l'échange



Musée des Confluences



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