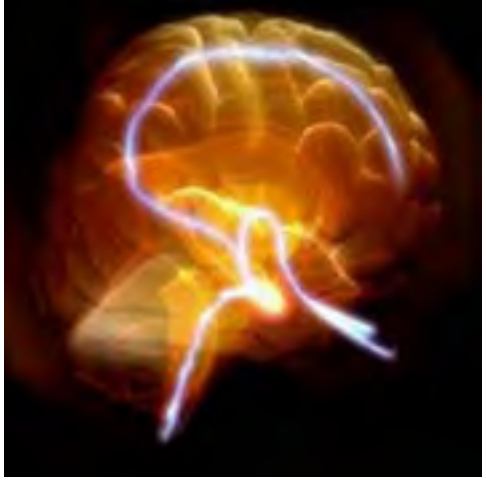
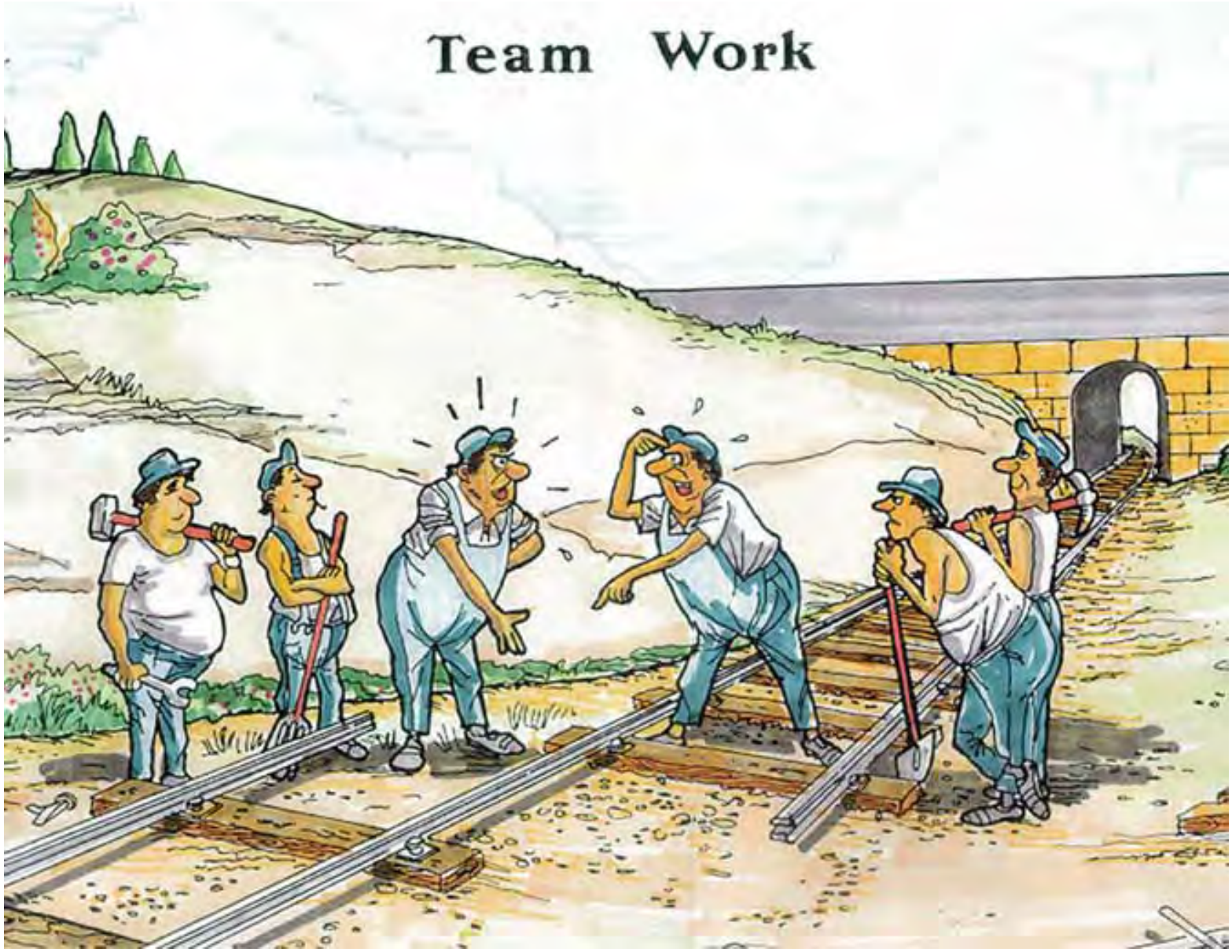
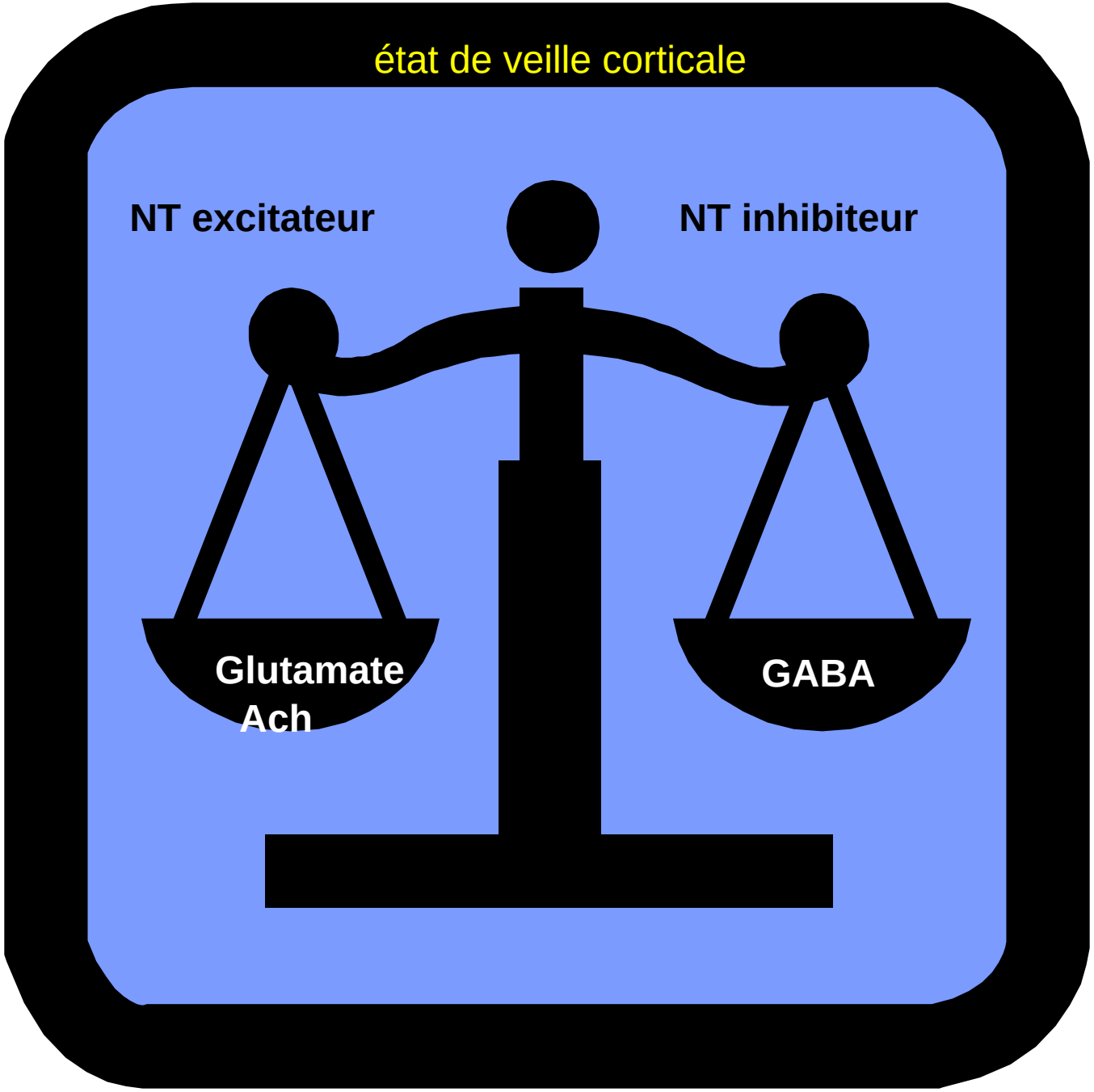


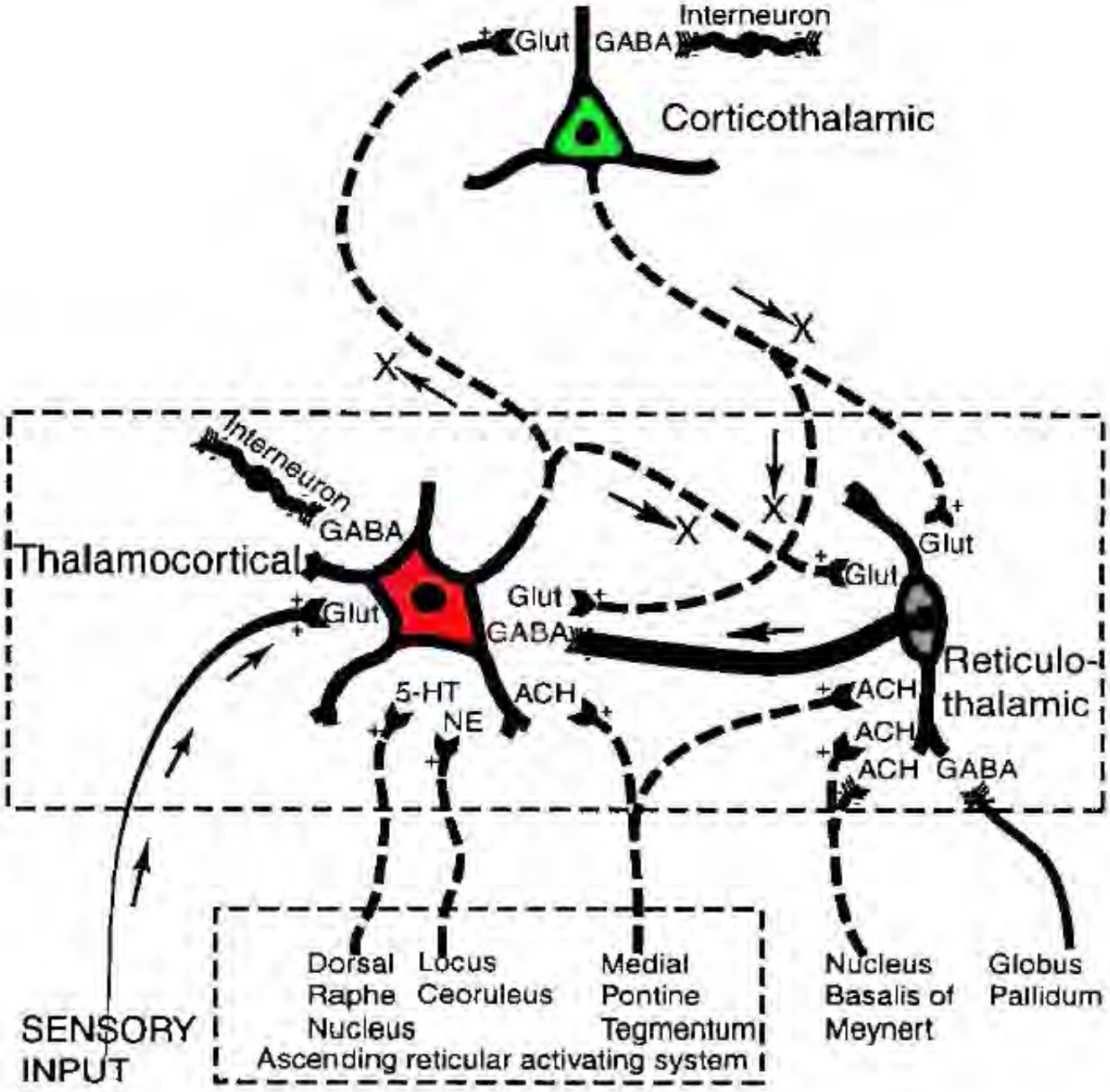
... Isoflurane et Sevoflurane se baladent dans le cerveau des enfants ...

Laure Pain, Neuro-4, CRBS, Inserm Strasbourg

Team Work

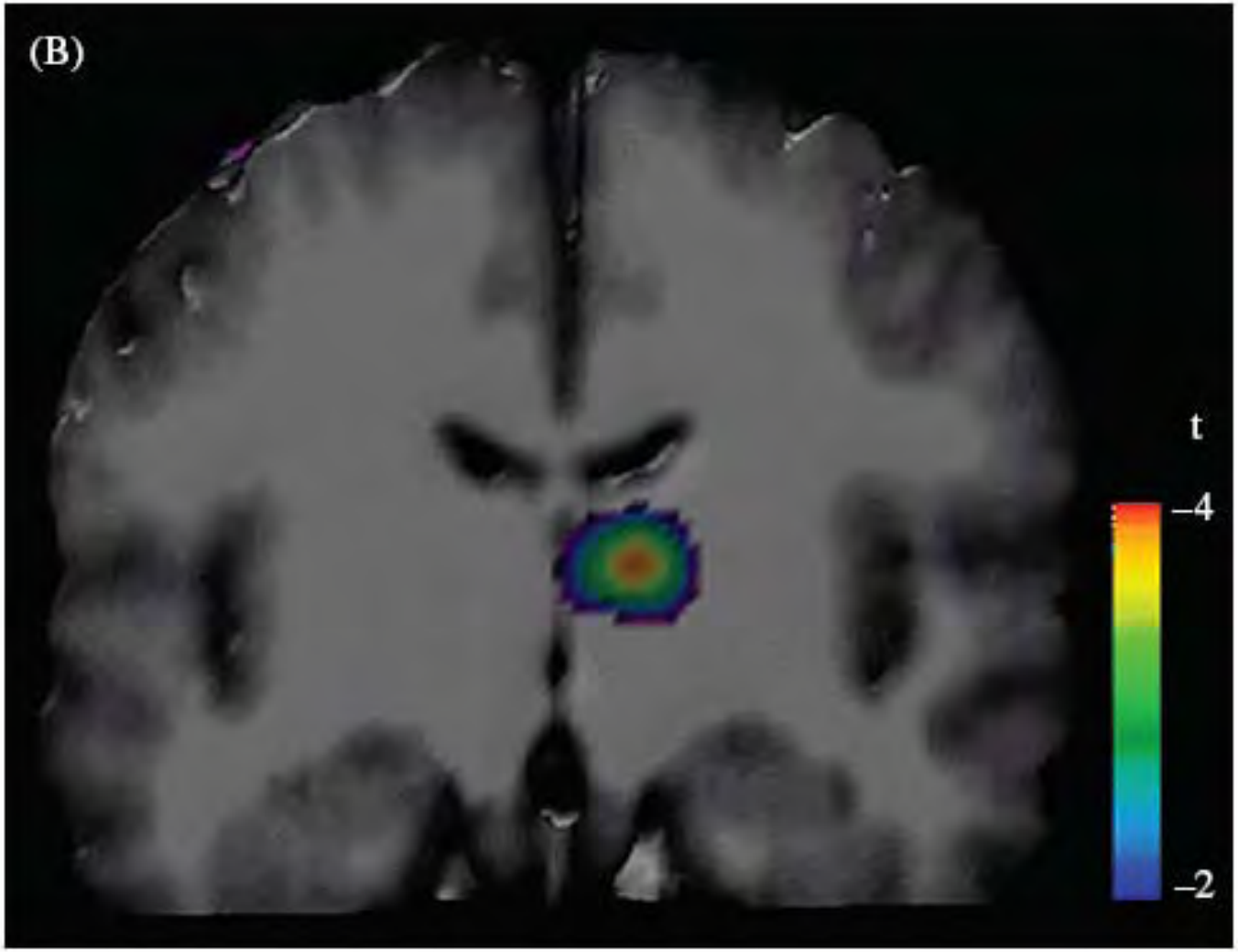



état de veille corticale
NT excitateur
NT inhibiteur
Glutamate
Ach
GABA


Interneuron
Glut
GABA
Corticothalamic
Interneuron
GABA
Thalamocortical
Glut
Glut
GABA
Glut
Glut
Reticulo-
thalamic
5-HT
NE
ACH
ACH
ACH
ACH
GABA
SENSORY
INPUT
Dorsal
Raphe
Nucleus
Locus
Ceoruleus
Medial
Pontine
Tegmentum
Ascending reticular activating system
Nucleus
Basalis of
Meynert
Globus
Pallidum

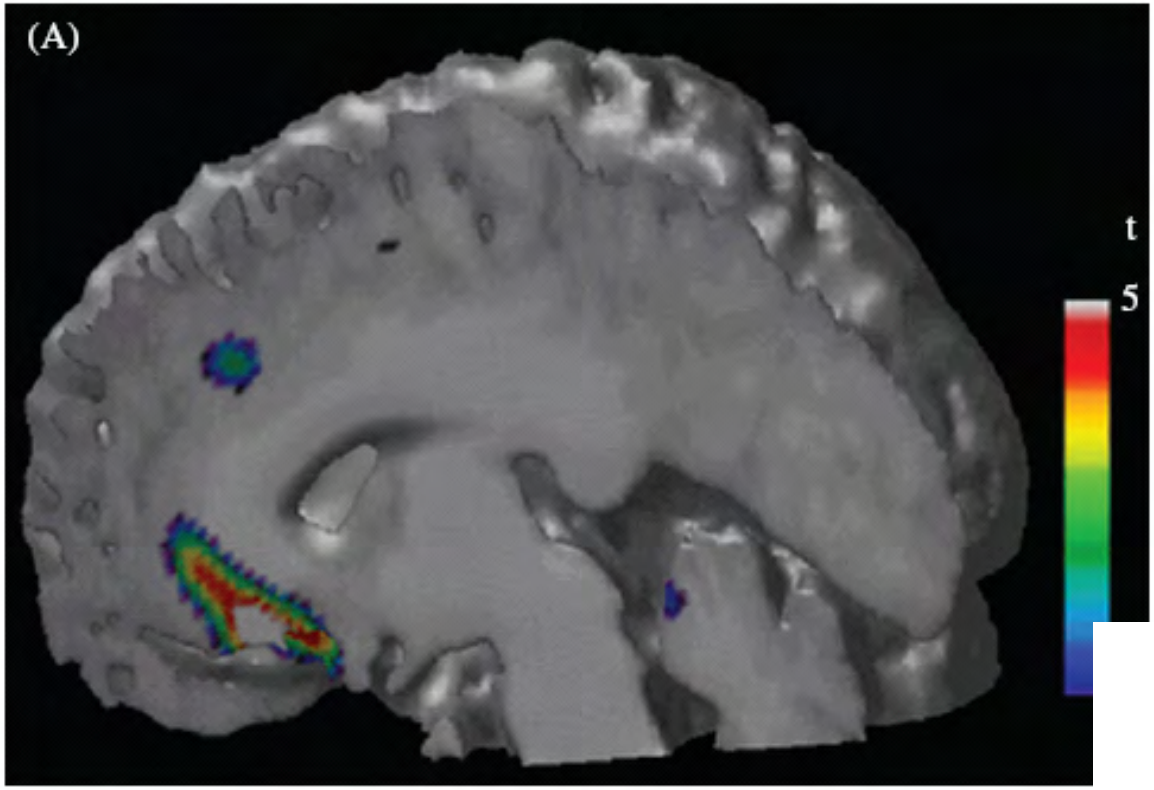
- aire cingulaire antérieure et insula ?

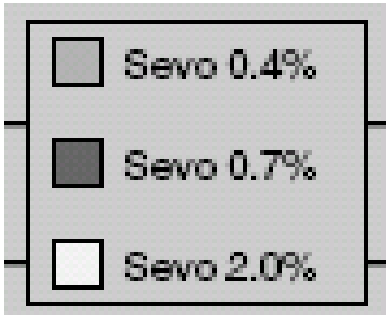
1 MAC SEVOFLURANE versus AWAKE

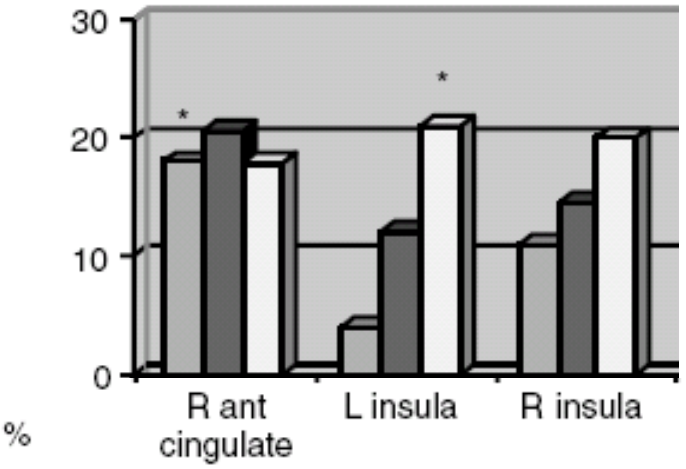


diminution rCBF dans le thalamus

1 MAC SEVOFLURANE



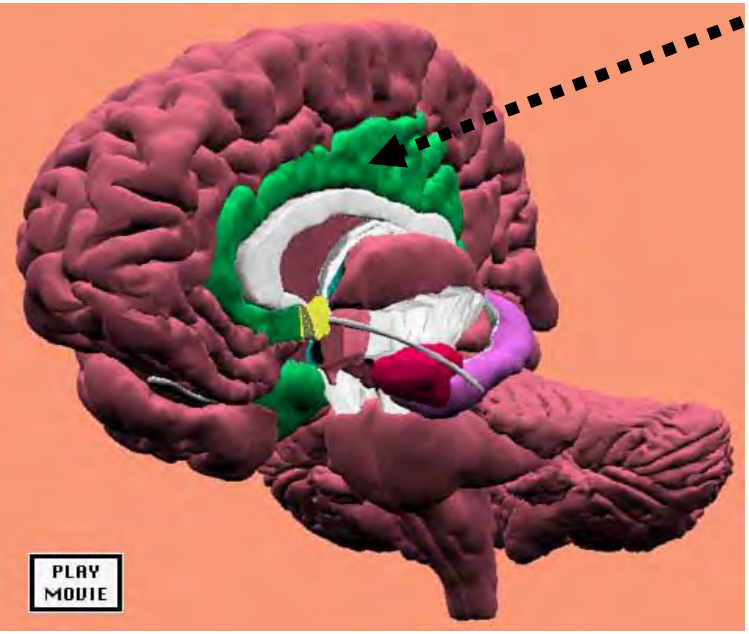


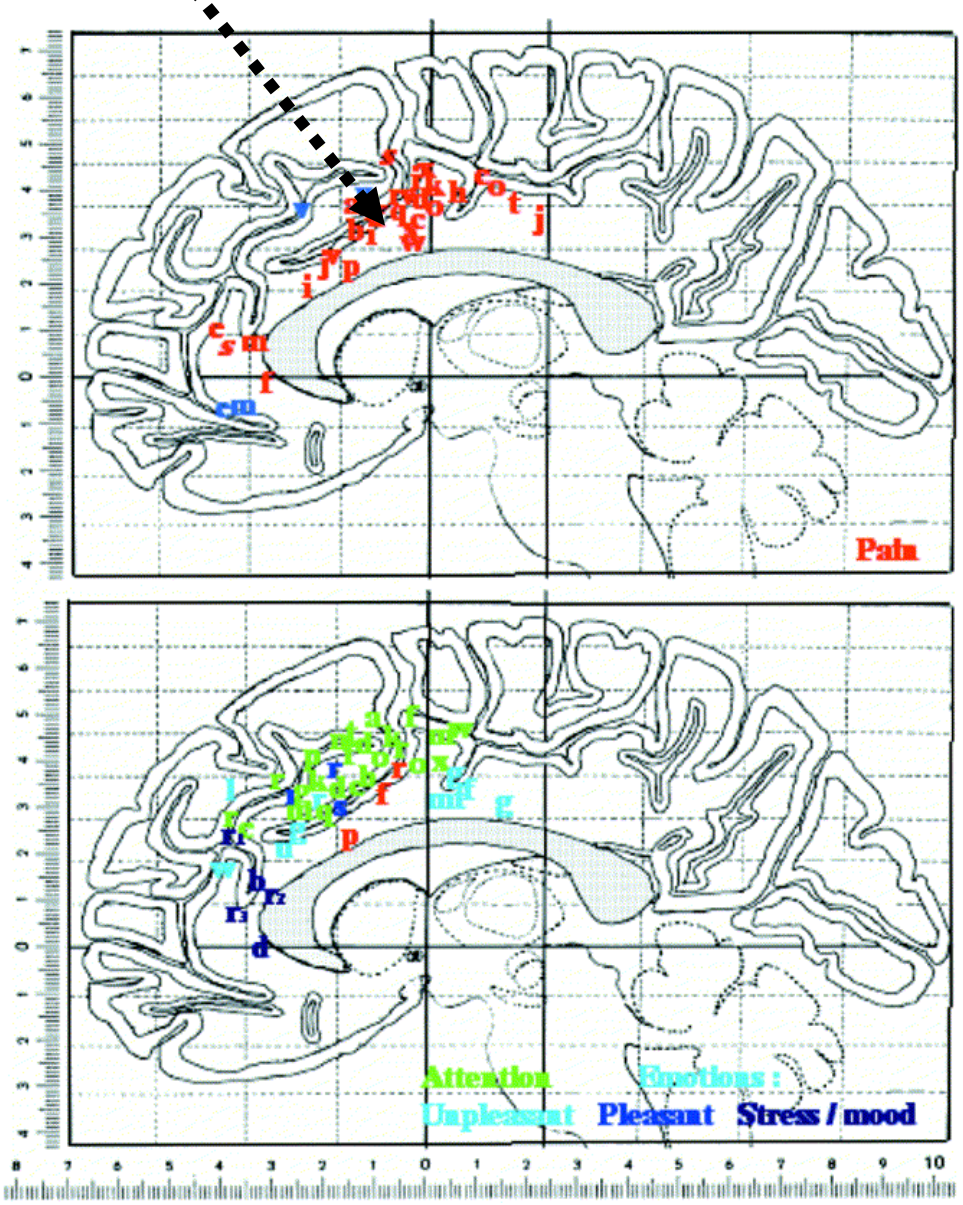


augmentation rCBF

- **aire cingulaire antérieure**
- **insula**

Cingulate area

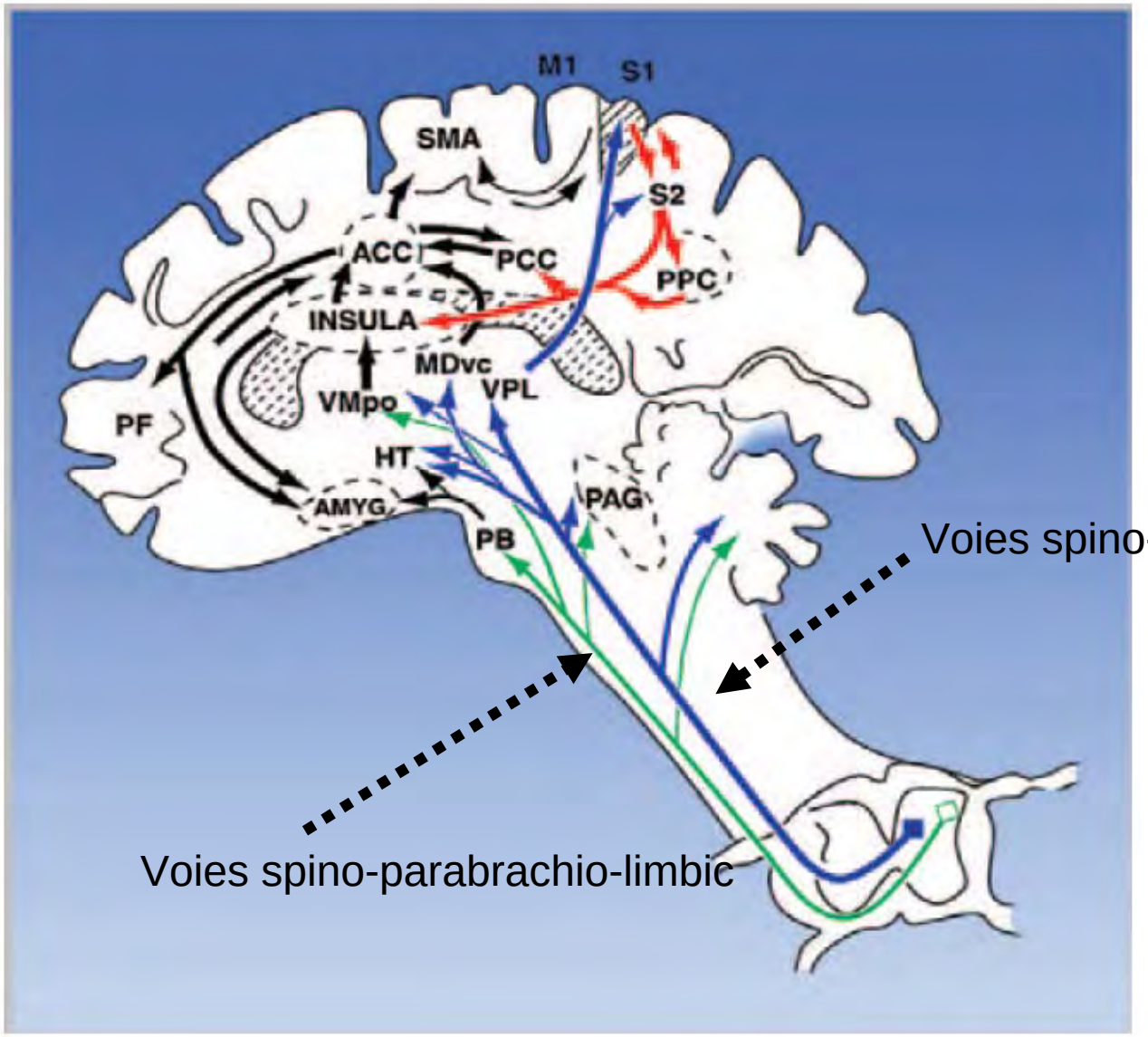




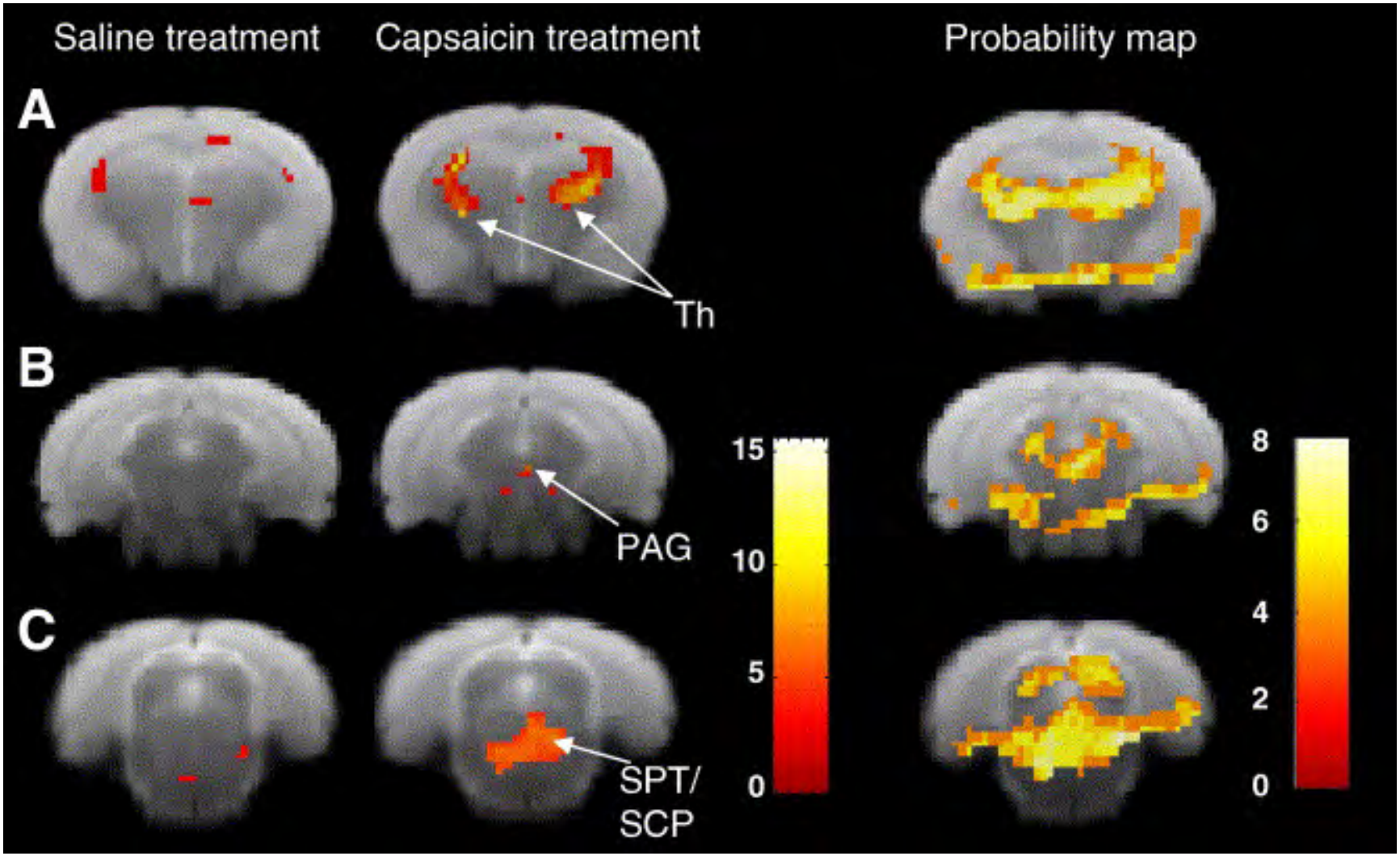
A role for

- affective component

Meta-analysis


M1
S1
SMA
S2
ACC
PCC
PPC
INSULA
MDvc
VPL
VMpo
PF
HT
AMYG
PAG
PB
Voies spino-thalamo-corticales
Voies spino-parabrachio-limbic

capsaine sous isoflurane 3-1,5 % et N202



- Locus Coeruleus ? transmission norodrénergique

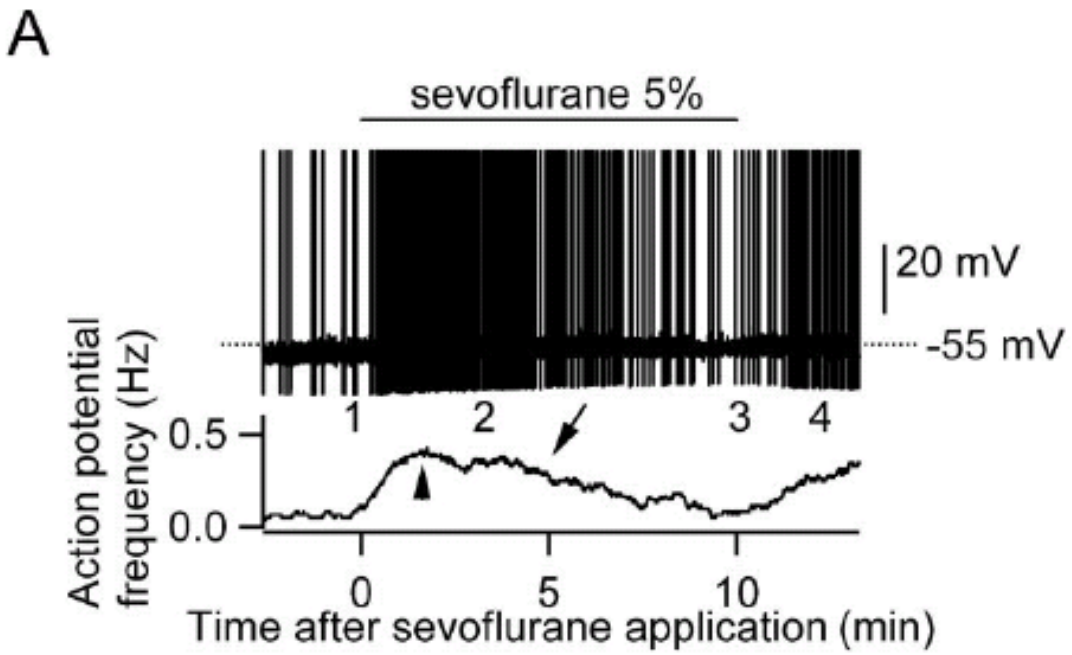
  ..... agitation, delirium d'émergence

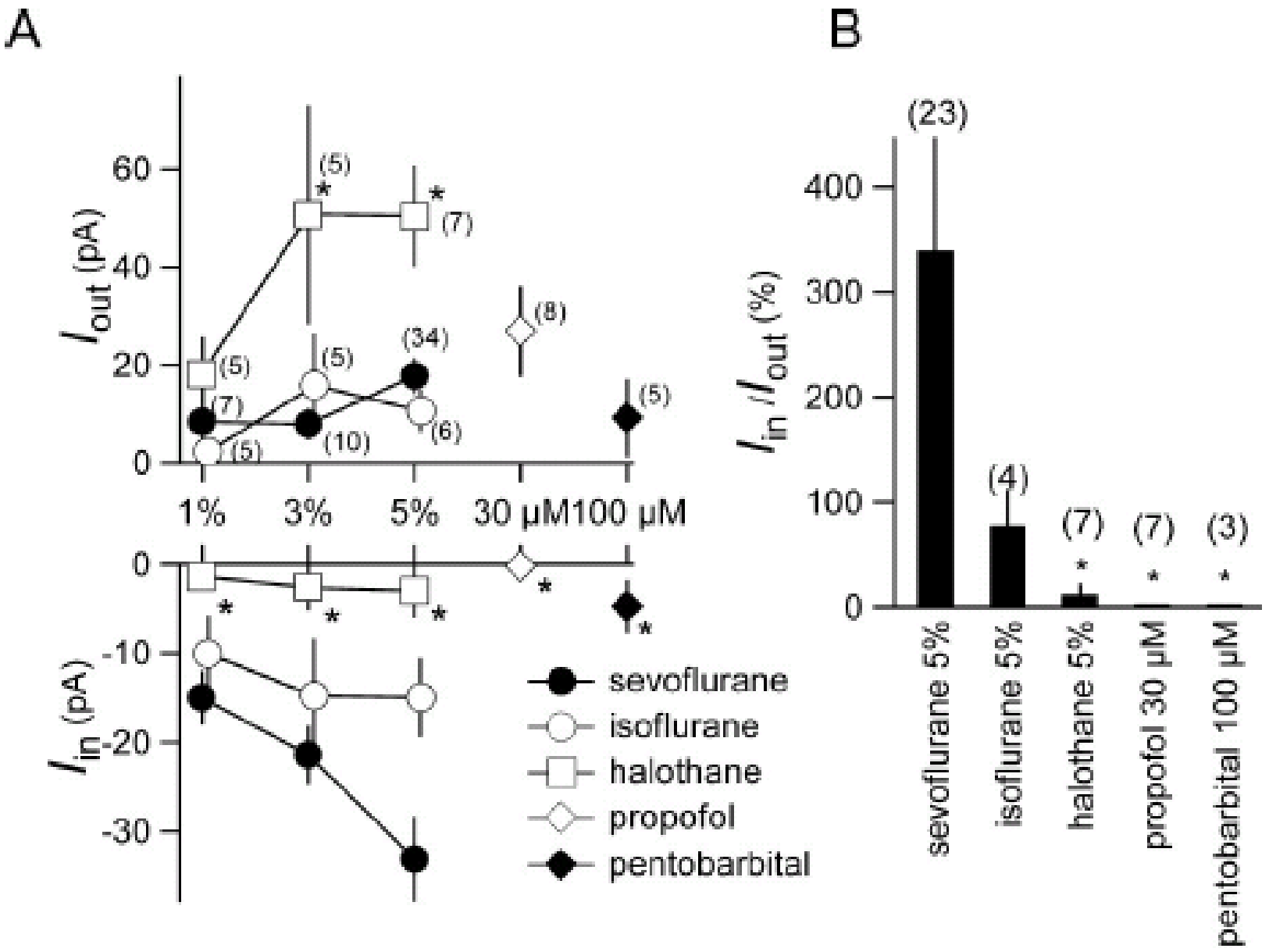
  ..... épileptogéne ?

Anesthesiology 2007; 107:992–1002
Copyright © 2007, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Sevoflurane Directly Excites Locus Coeruleus Neurons of Rats

Yutaka Yasui, M.D., Eiji Masaki, M.D., Ph.D.,† Fusao Kato, Ph.D.‡*




A
B
I_{out} (pA)
I_{in} (pA)
I_{in} / I_{out} (%)
1%
3%
5%
30 µM
100 µM
sevoflurane
isoflurane
halothane
propofol
pentobarbital
sevoflurane 5%
isoflurane 5%
halothane 5%
propofol 30 µM
pentobarbital 100 µM

Regarding sevoflurane and emergence agitation…again!

Alpha2 centraux …
Ketamine …
Physostigmine …
Midazolam …
Propofol …

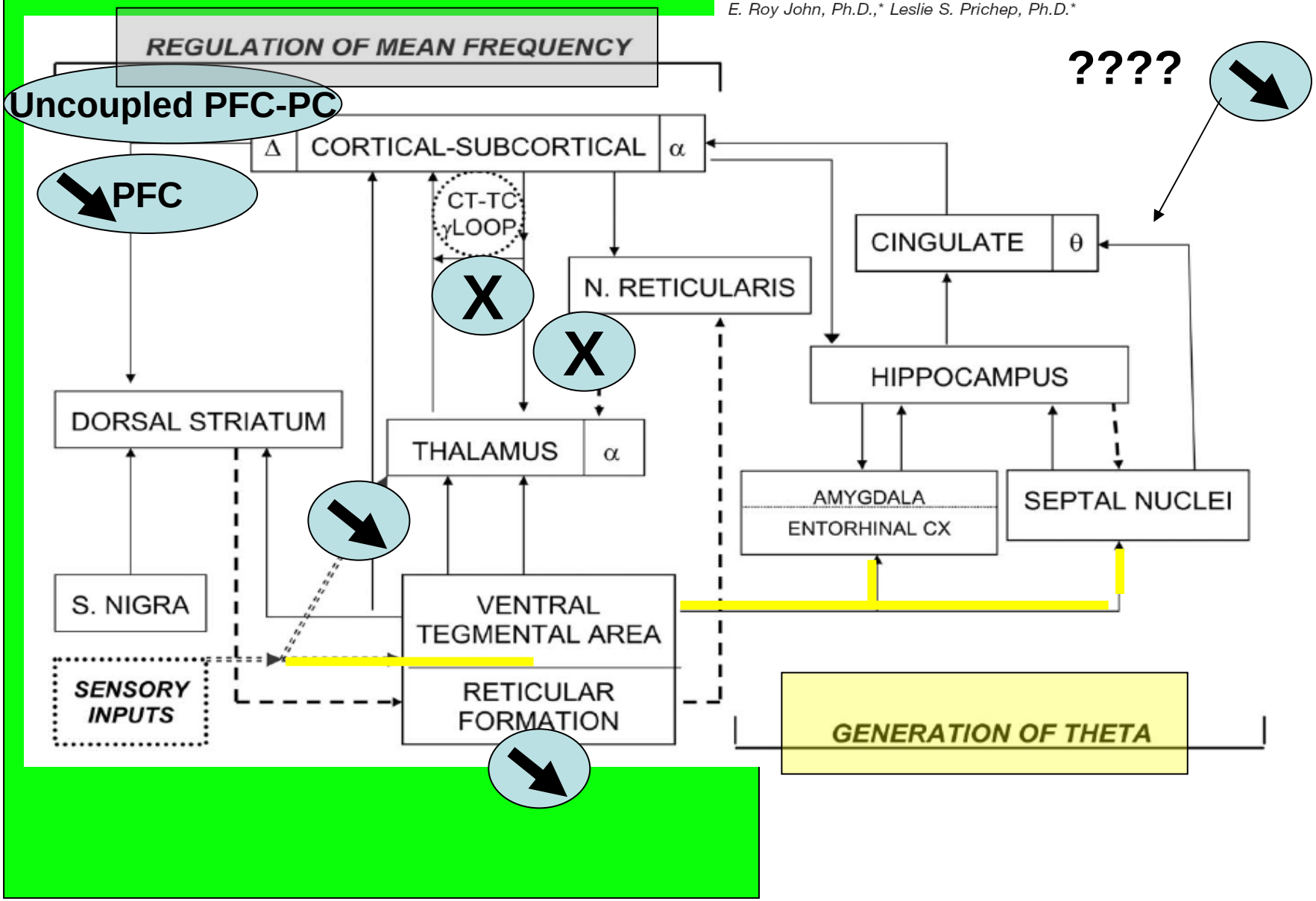
... and what else ? ...

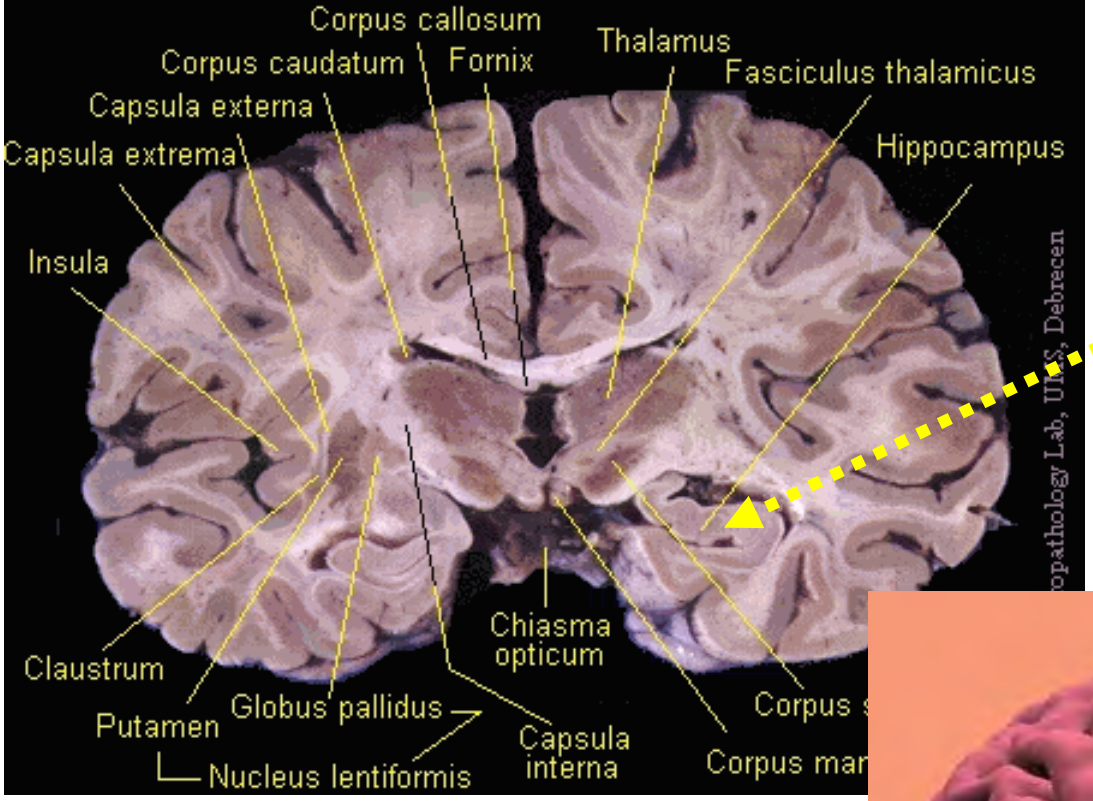
Anesthesiology 2005; 102:447–71
© 2005 American Society of Ane

The Anesthetic Cascade

A Theory of How Anesthesia Suppresses Consciousness

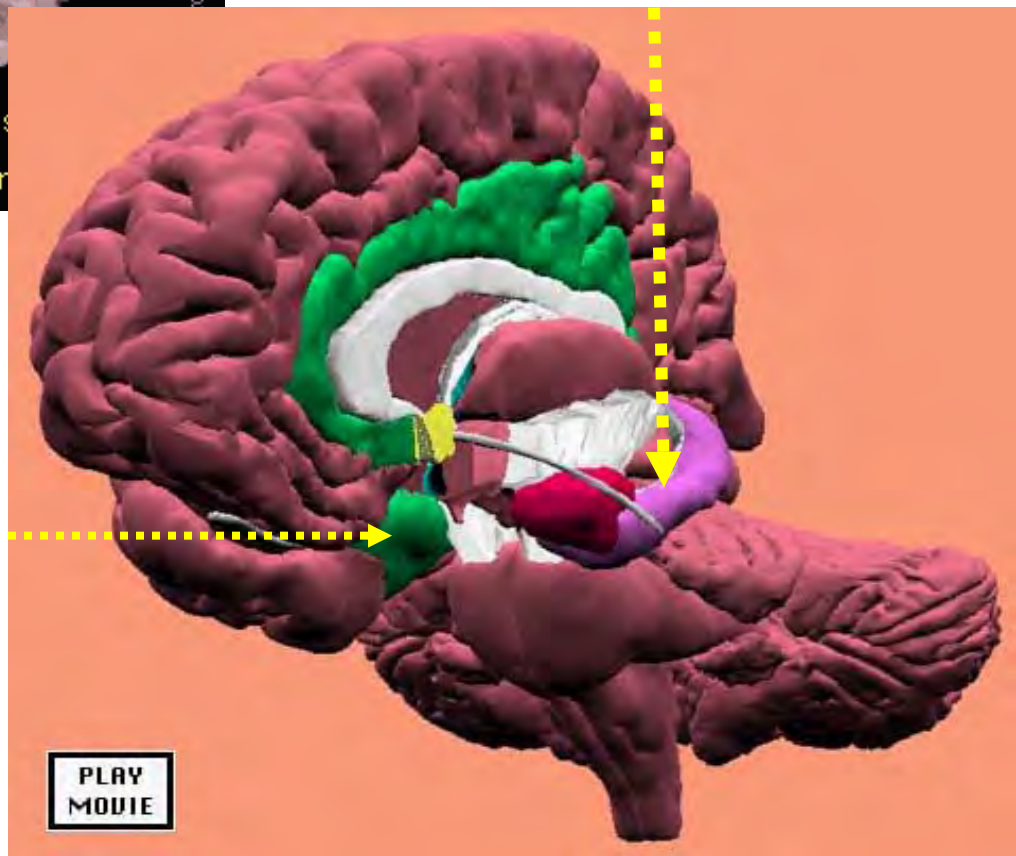
E. Roy John, Ph.D., Leslie S. Prichep, Ph.D.**





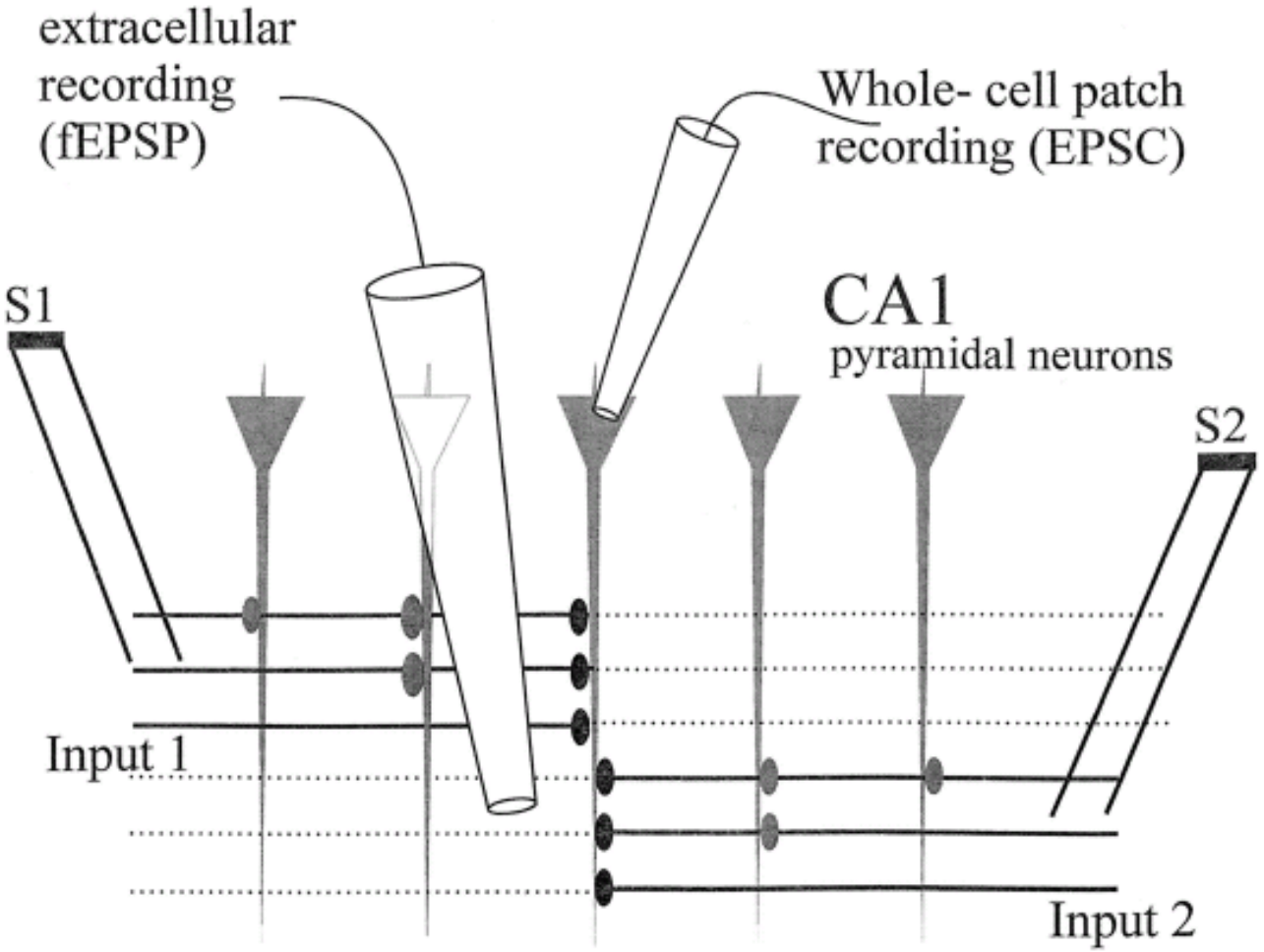
Hippocampal formation

Parahippocampal girus

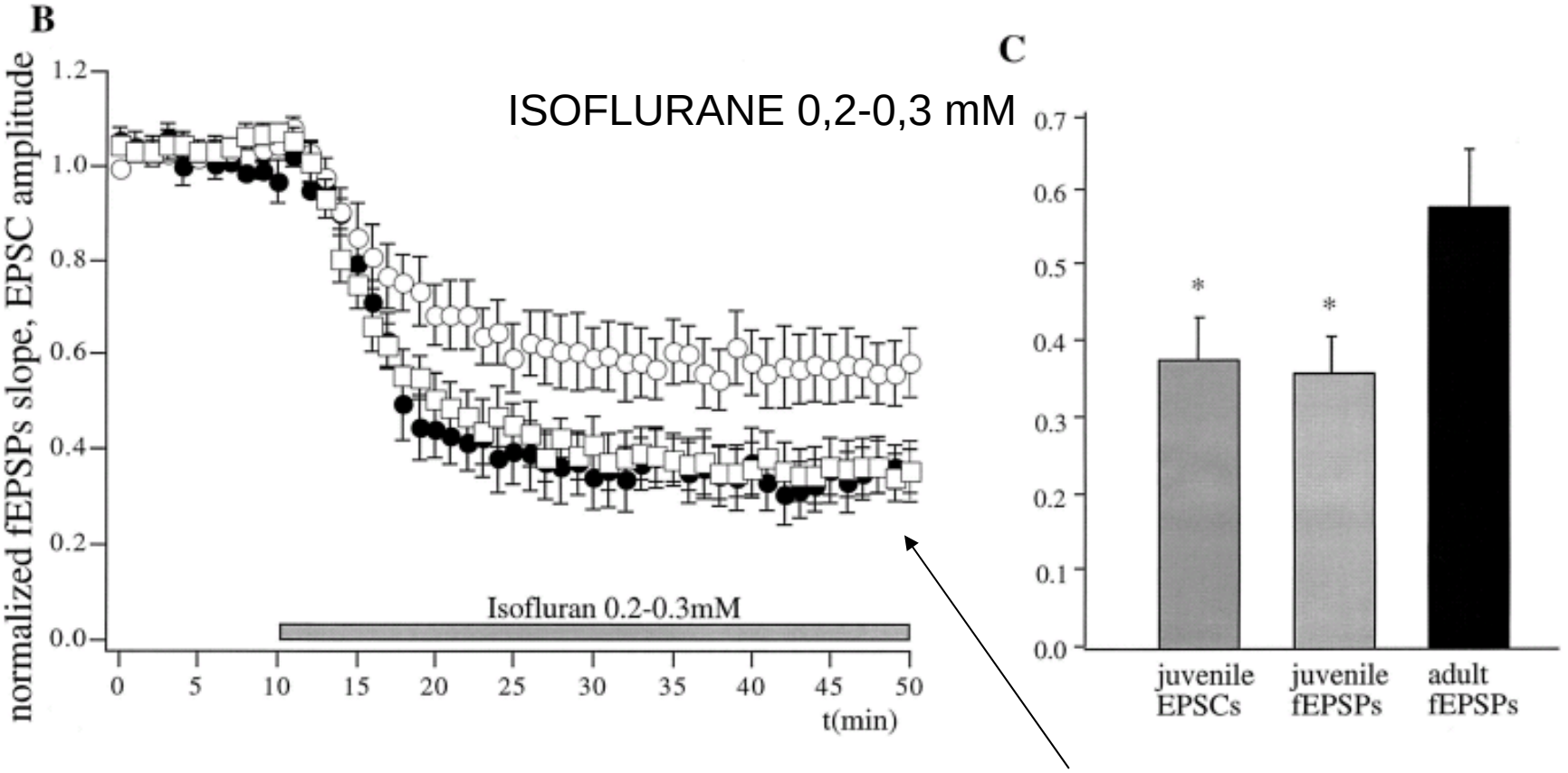


Anesthesiology 2001; 94:1058–65
© 2001 American Society of Anesthesiologists, Inc. Lippincott

Isoflurane Blocks Synaptic Plasticity in the Mouse Hippocampus



hippocampe
transmission excitatrice glutamate



ISOFLURANE 0,2-0,3 mM

courant AMPA-kainate post synaptique

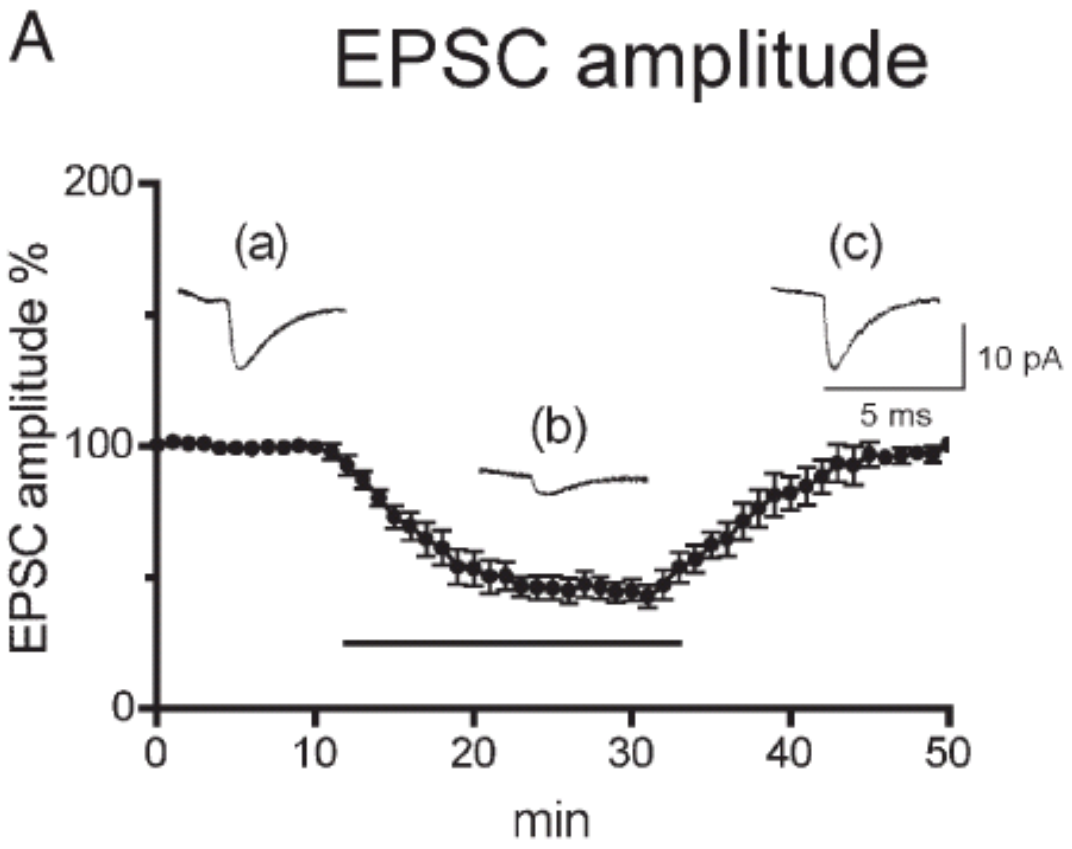
Research Report

Brain Research 2008, 32-39

Facilitatory effects of subanesthetic sevoflurane on excitatory synaptic transmission and synaptic plasticity in the mouse hippocampal CA1 area

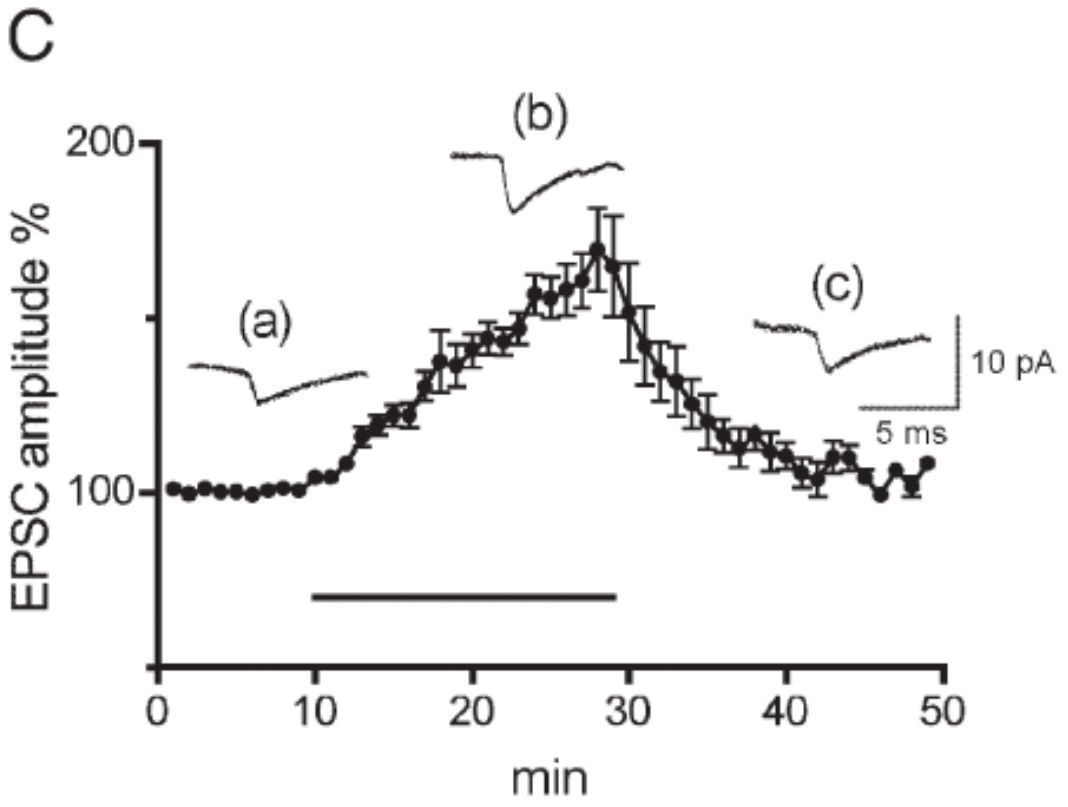
*Toshiki Otsubo, Masao Maekawa, Toshiaki Nagai, Hideaki Sakio, Yuuichi Hori**

SEVOFLURANE 0,5 mM



Effet facilitateur à faible dose (équivalent 0,3-0,5 % humain)

SEVOFLURANE
0,05 mM



Diminution de la valence émotionelle de mots

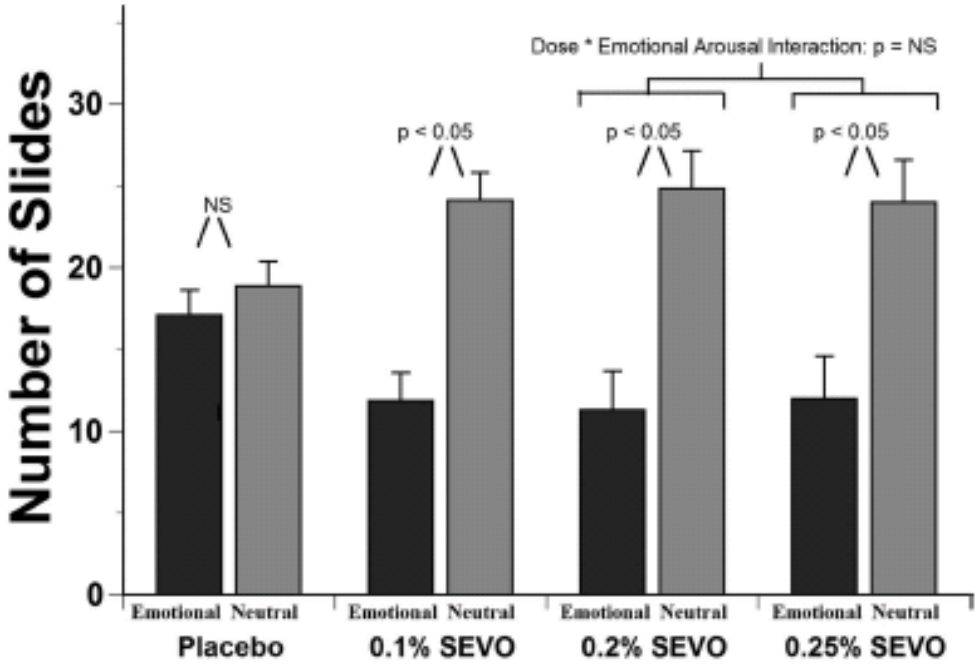
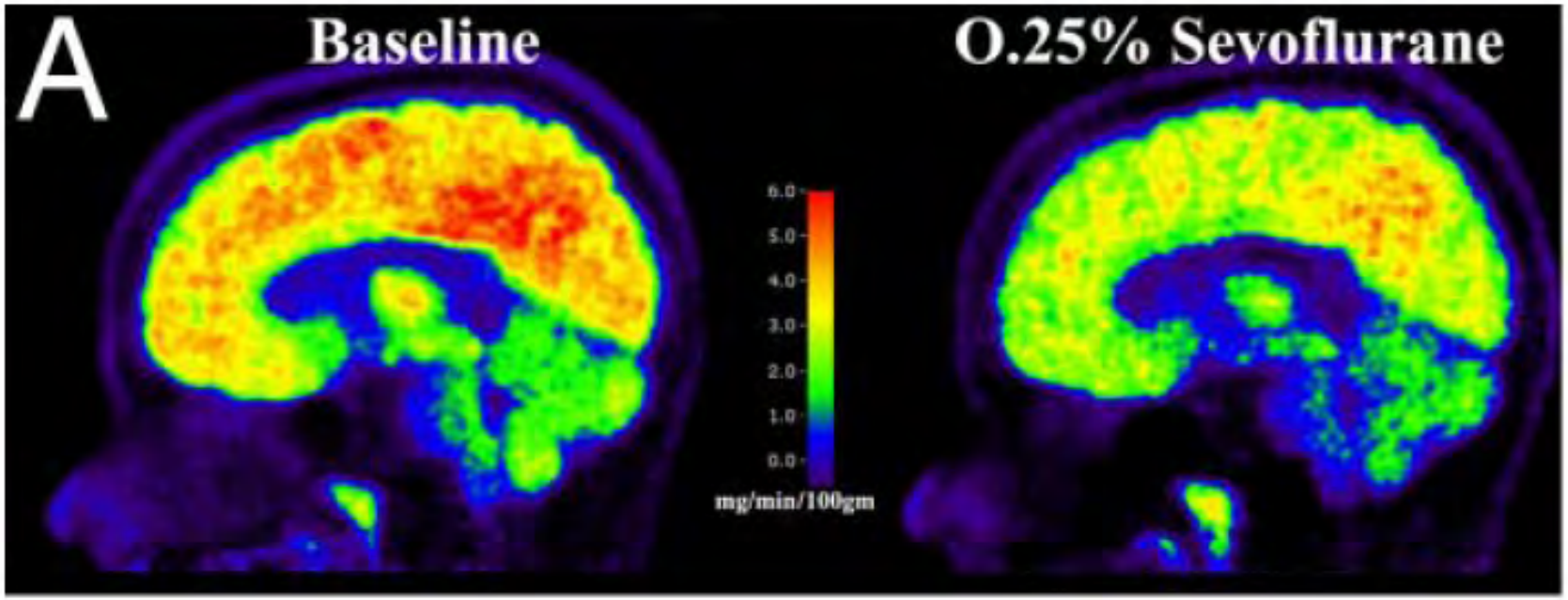


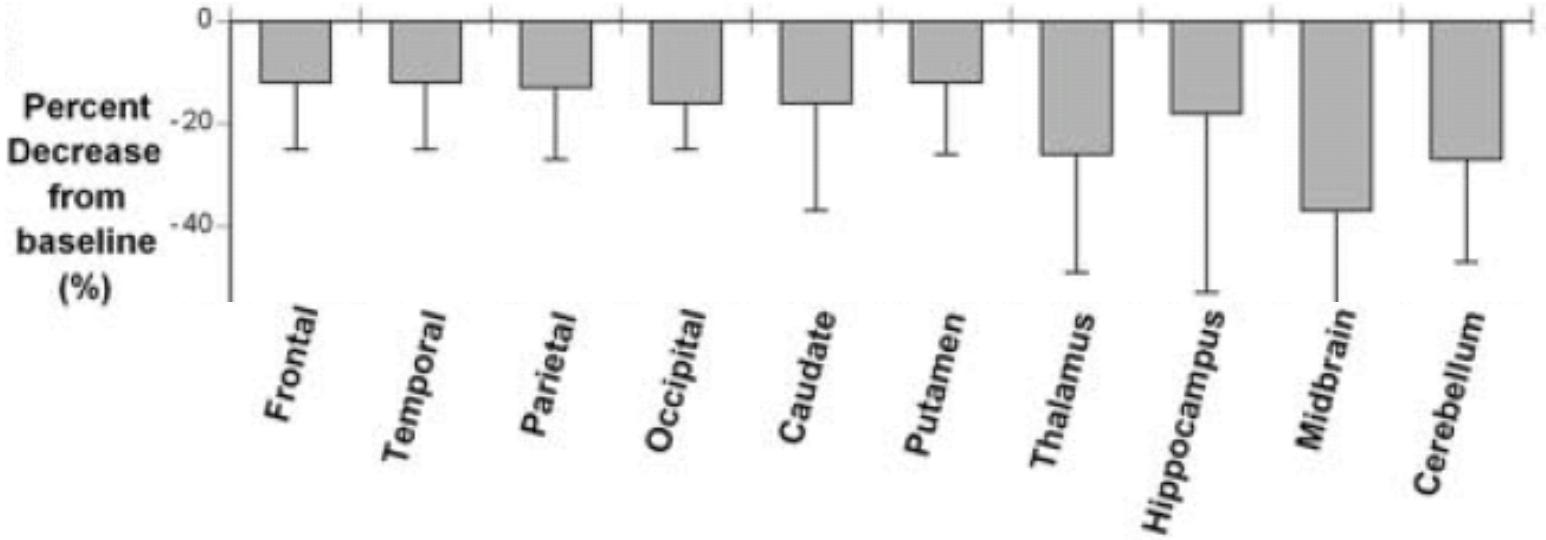
FIg. 1. The number of pictures rated as either neutral or emotional for their arousal reaction is shown (mean ± SEM). Placebo subjects rated the same number of items neutral as emotional. Subjects that received sevoflurane (SEVO) rated significantly more items as neutral vs. emotional. There was no significant effect of increasing dose from 0.2% to 0.25% on how subjects rated the pictures, as shown by the dose × emotionality interaction. NS, not significant.

Neuroimaging analysis of an anesthetic gas that blocks human emotional memory

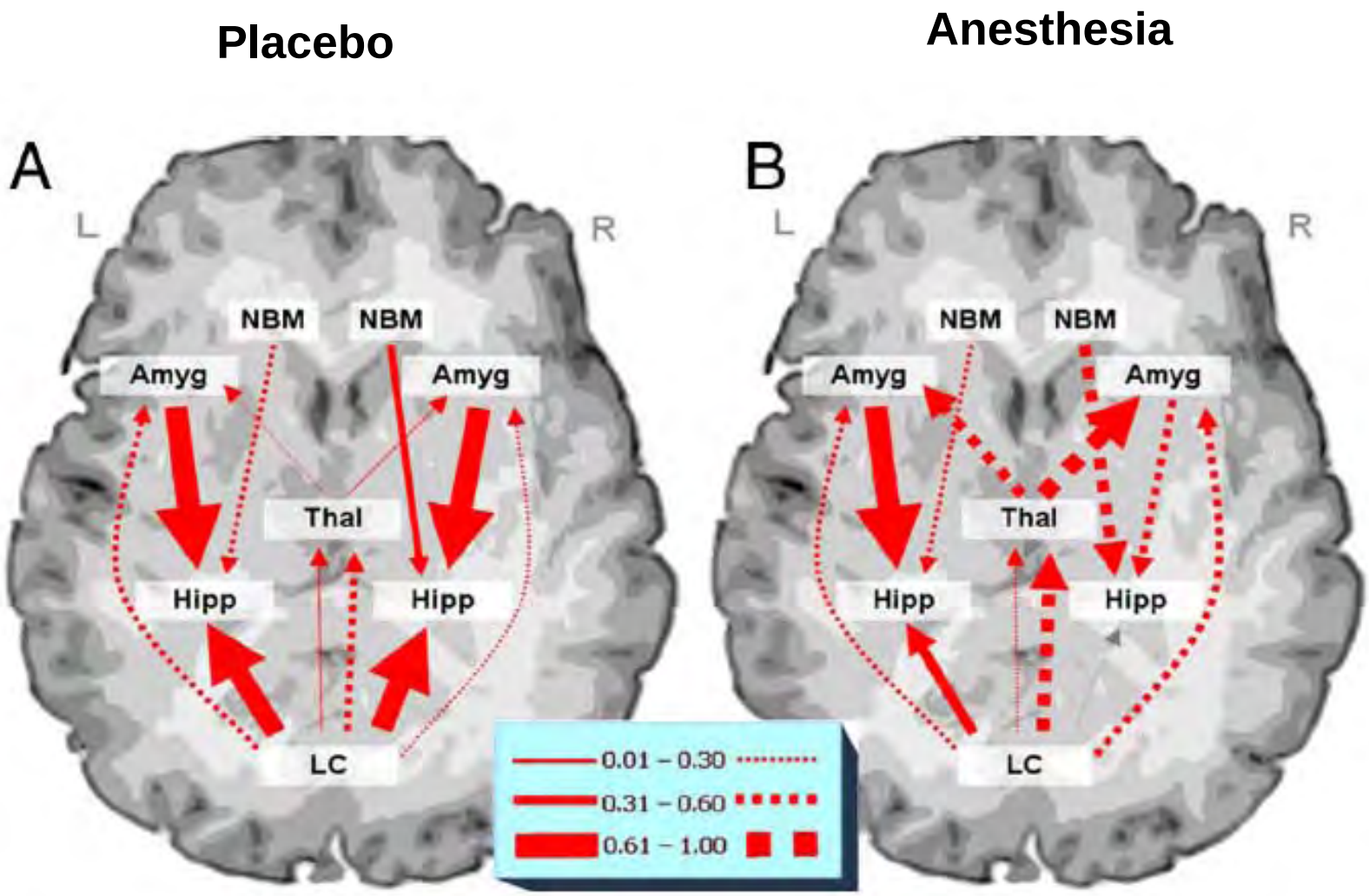
Michael T. Alkire*†‡, Robin Gruver*, Jason Miller*, Jayme R. McReynolds*, Emily L. Hahn*, and Larry Cahill†§

1722–1727 | PNAS | February 5, 2008 | vol. 105 | no. 5


A
Baseline
O.25% Sevoflurane
6.0
5.0
4.0
3.0
2.0
1.0
0.0
mg/min/100gm

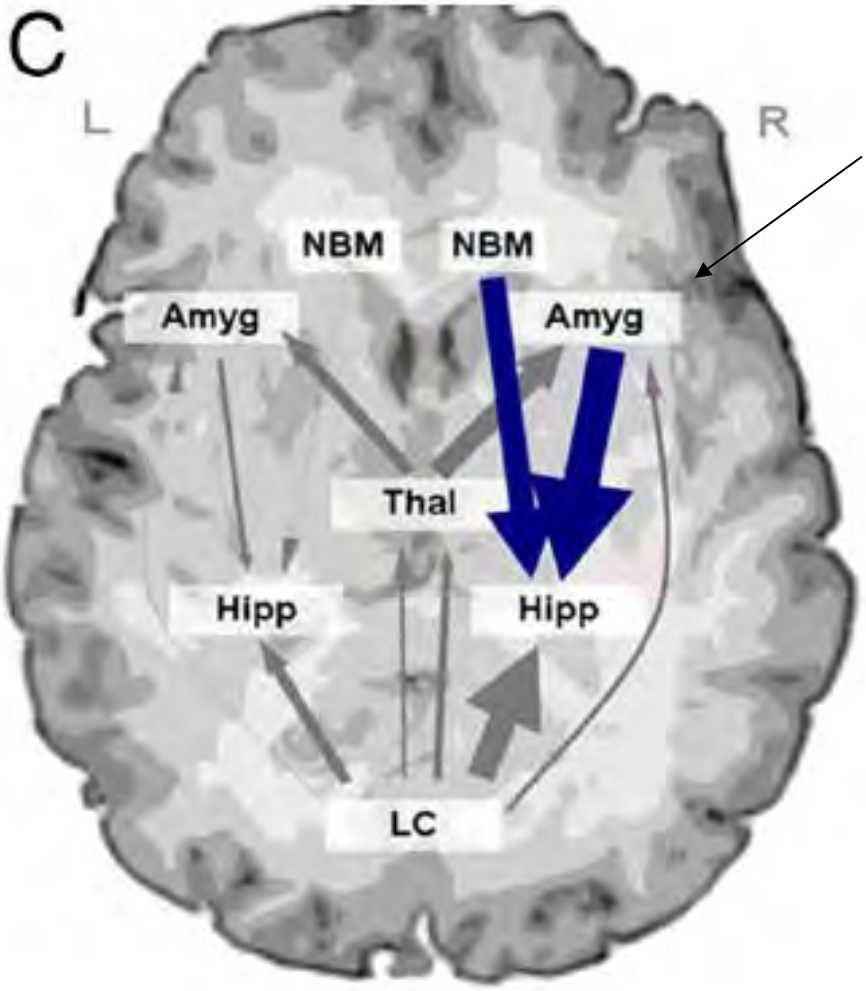

Percent Decrease from baseline (%)
0
-20
-40
Frontal
Temporal
Parietal
Occipital
Caudate
Putamen
Thalamus
Hippocampus
Midbrain
Cerebellum

Mémorisation de mot à connotation émotionelle

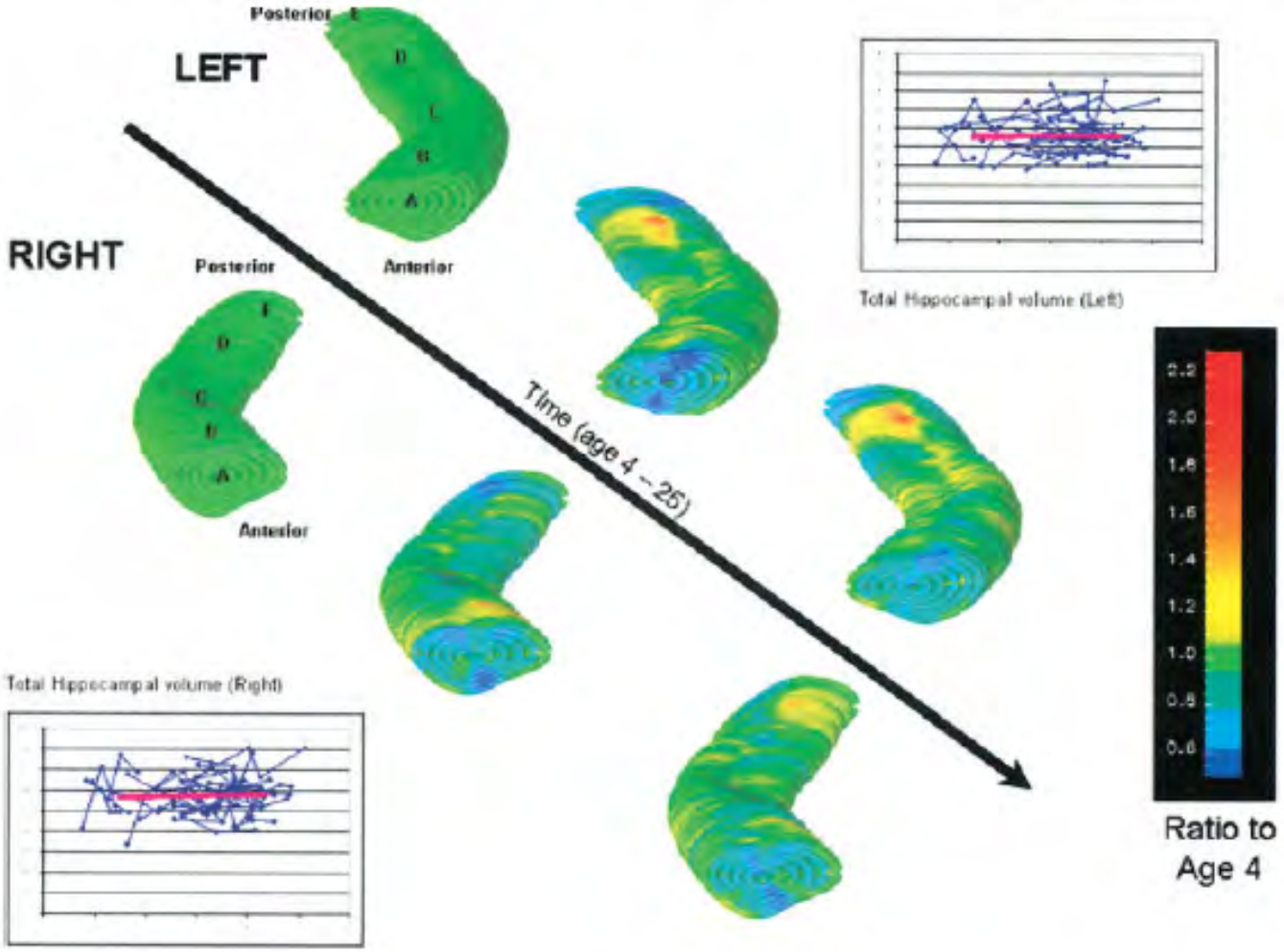


influence positive

influence négative



Sévoflurane 0,25 %
bloque l'effet facilitateur
de l'amygdale (émotion)
et NBM (attention)
sur l'intégration et la mémorisation
par l'hippocampe
d'un mot à valence affective


LEFT
RIGHT
Posterior
Anterior
Posterior
Anterior
Time (age 4 ~ 25)
Total Hippocampal volume (Left)
Total Hippocampal volume (Right)
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
Ratio to Age 4

Anaesthesia, 2007, **62**, pages 778–789 doi:10.1111/j.1365-2044.2007.05133.x

Intra-operative awareness in children: the value of an interview adapted to their cognitive abilities

U. Lopez,[1] W. Habre,[2] M. Laurençon,[1] G. Haller,[3] M. Van der Linden[4] and I. A. Iselin-Chaves[3]

1,15 % environ mémorisation explicite
mémorisation implicite ??

British Journal of Anaesthesia **100 (3):** 389–96 (2008)
doi:10.1093/bja/aem378 Advance Access publication January 25, 2008

BJA

PAEDIATRICS

Awareness and memory function during paediatric anaesthesia

J. Andrade[1]*, C. Deeprose[2] and I. Barker[3]

pas de mémorisation implicite pour mots neutres

Anaesthesia, 2008, **63**, pages 474–481 doi:10.1111/j.1365-2044.2007.05412.x

Intra-operative awareness in children and post-traumatic stress disorder*

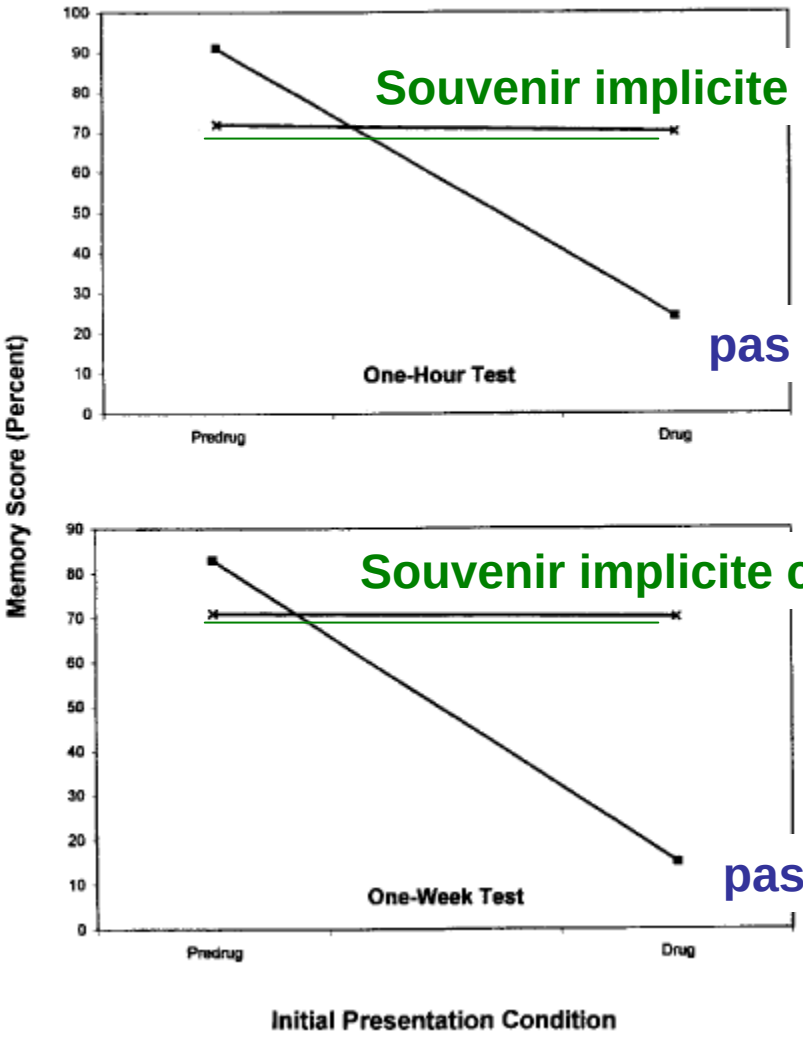
U. Lopez,[1] W. Habre,[2] M. Van der Linden[3] and I. A. Iselin-Chaves[4]

1 Psychologist, Division of Anaesthesiology, Pharmacology and Intensive Care, University Hospital of Geneva, 2 Senior Consultant, Paediatric Anaesthesia Unit, University Hospital of Geneva, 3 Professor of Psychology, Cognitive Psychopathology and Neuropsychology Unit, University of Geneva, and 4 Senior Registrar, Division of Anaesthesiology, University Hospital of Geneva, Geneva, Switzerland

pas de syndrome de stress post -traumatique

Sédation consciente chez enfants (ponction de moelle)

midazolam 0,10 à 0,15 mg/kg IV
et fentanyl 1 à 2 microg/kg



Souvenir implicite conservé

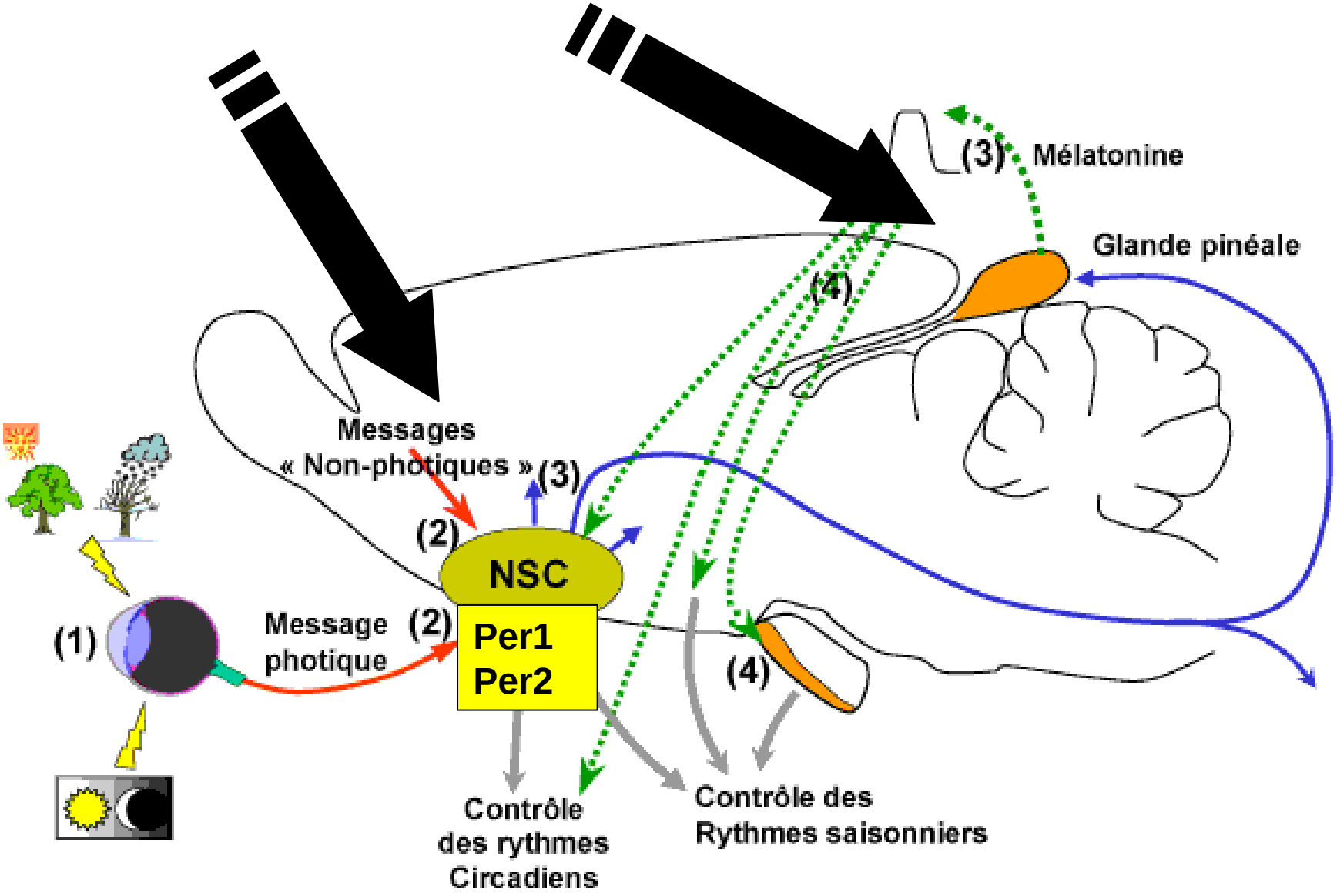
pas de souvenir explicite : « amnésie »

Souvenir implicite conservé

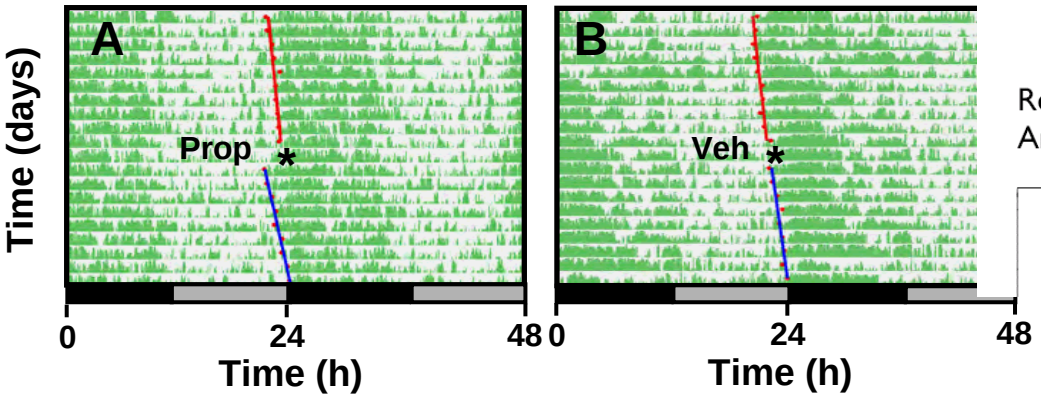
pas de souvenir explicite : « amnésie »

D'après Pringle et al. 2003

Les halogénés
et l’ horloge interne du cerveau


(3) Mélatonine
Glande pinéale
(4)
Messages
« Non-photiques »
(3)
(2)
NSC
Per1
Per2
(1)
Message
photique
(2)
(4)
Contrôle
des rythmes
Circadiens
Contrôle des
Rythmes saisonniers

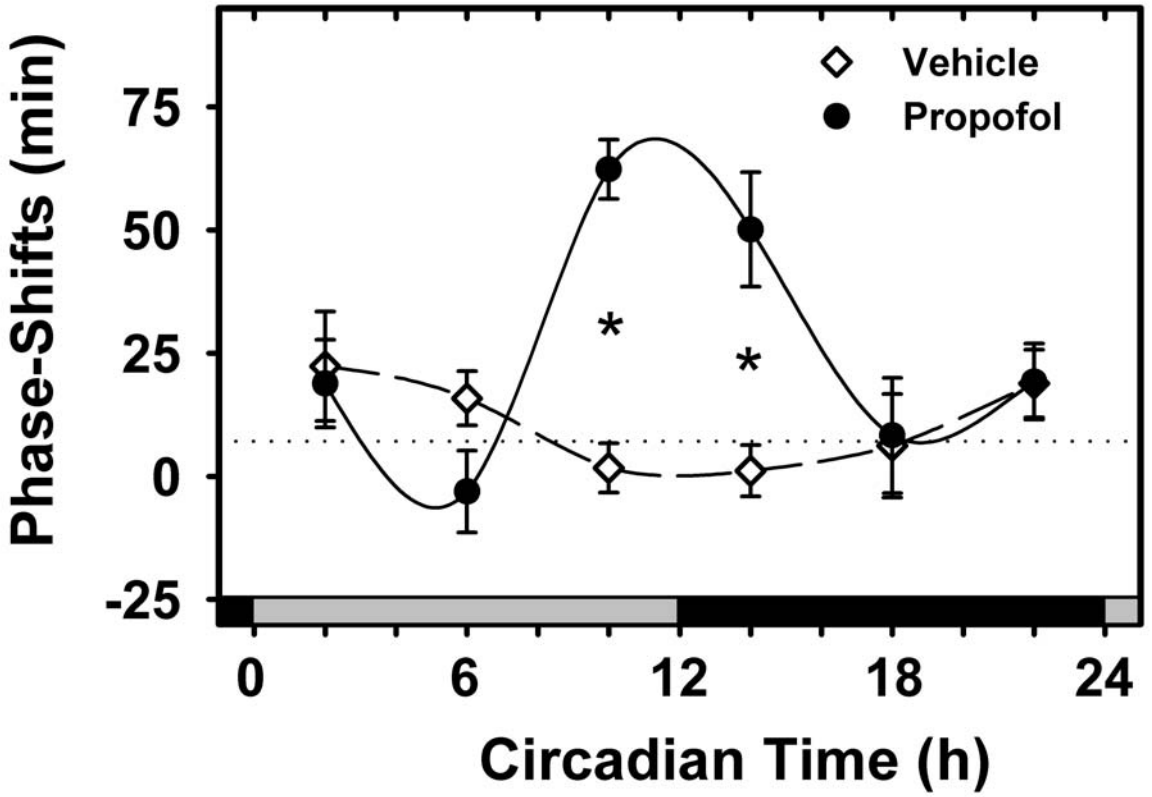
Neuropsychopharmacology (2006), 1–8
© 2006 Nature Publishing Group All rights reserved 0893-133X/06 $30.00
www.neuropsychopharmacology.org

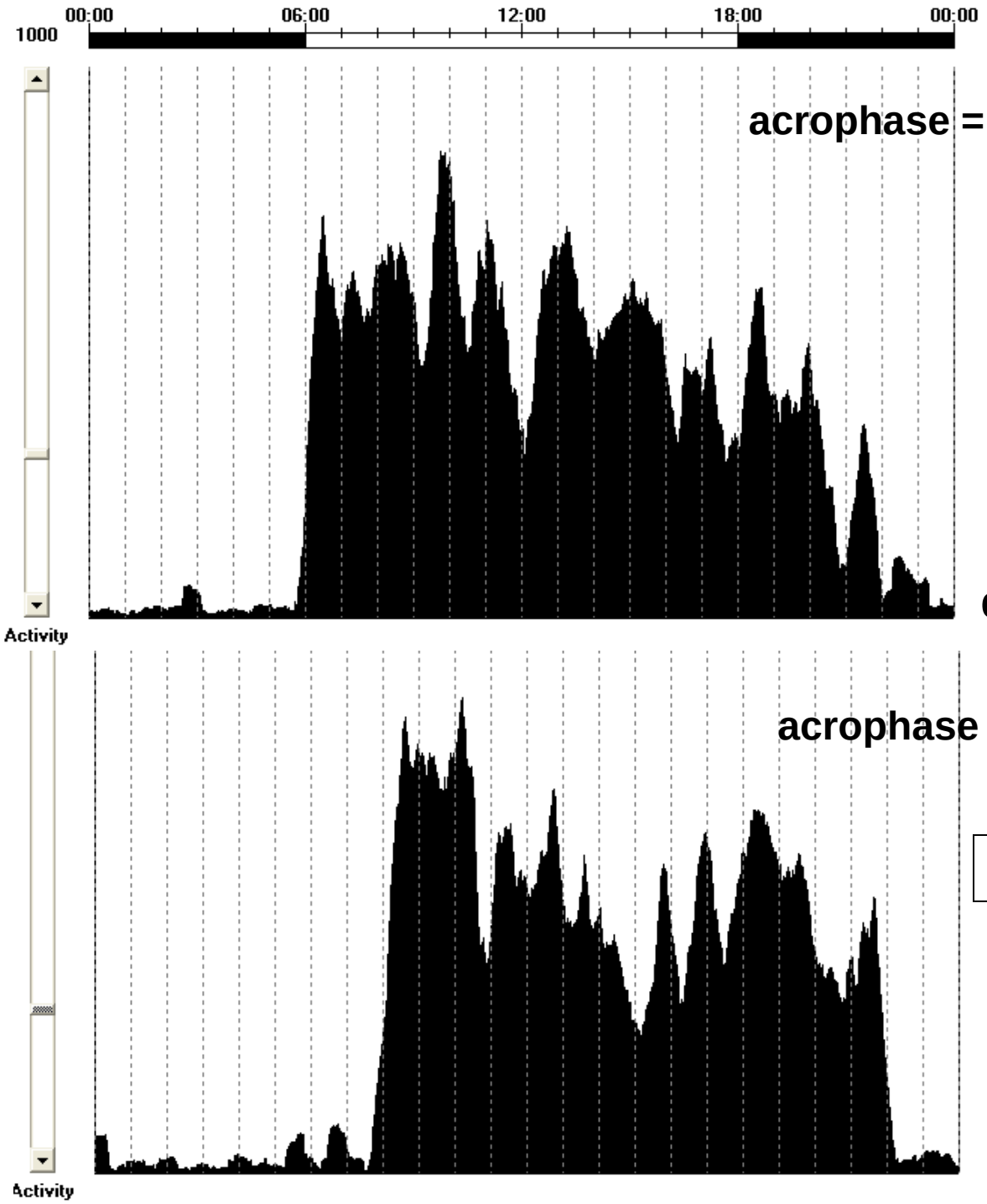


Reciprocal Relationships between General (Propofol) Anesthesia and Circadian Time in Rats

Etienne Challet[1,4], Sylviane Gourmelen[1], Paul Pevet[1], Philippe Oberling[2] and Laure Pain*[,3,4]

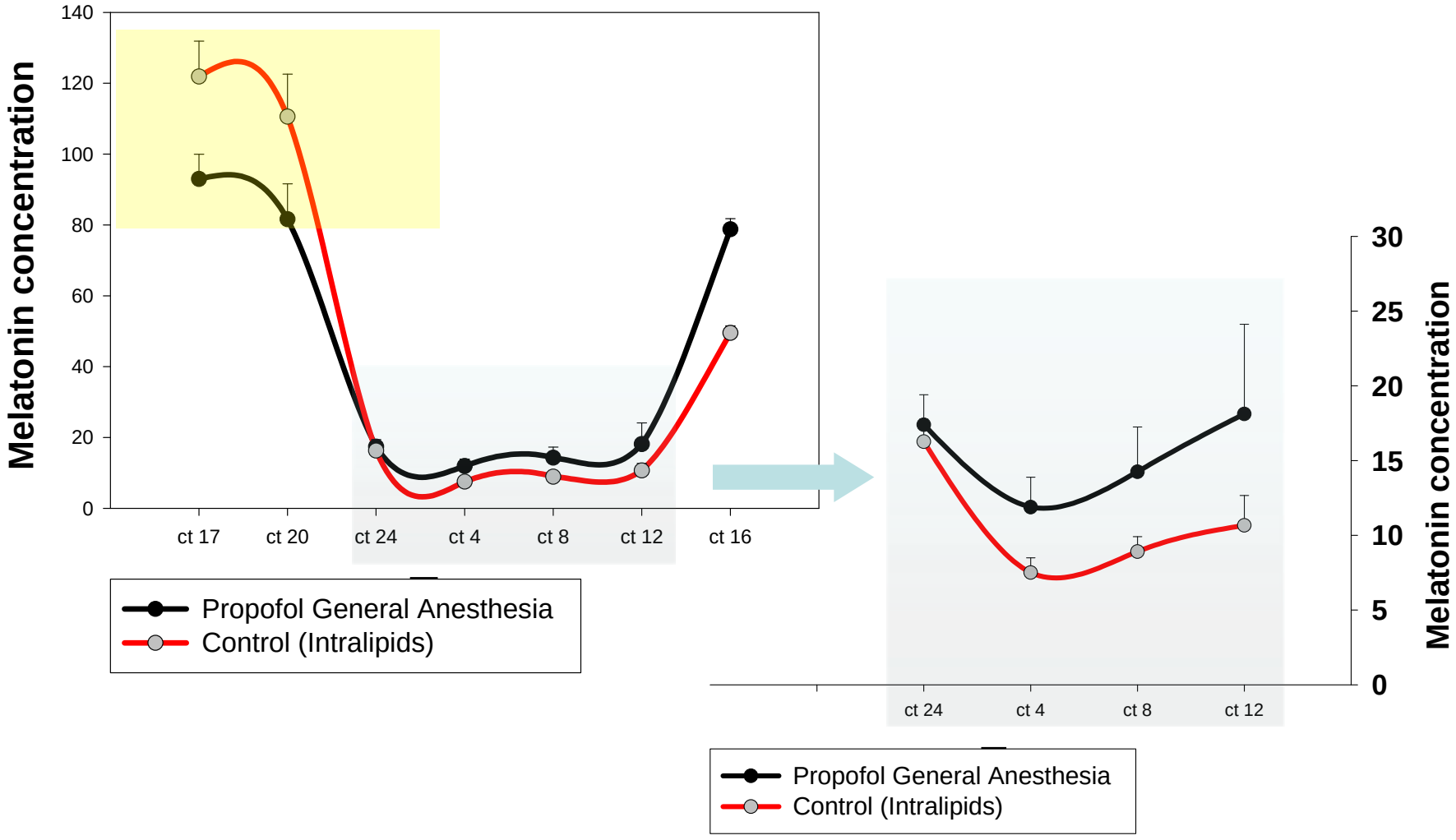
[1]*Department of Neurobiology of Rhythms, Institute of Cellular and Integrative Neurosciences, CNRS (UMR7168), University L. Pasteur, Strasbourg, France;* [2]*Laboratory of Behavioural and Cognitive Neuroscience, CNRS (FRE2855), University L. Pasteur, Strasbourg, France;* [3]*INSERM U666 (GRERCA) and Hôpitaux Universitaires de Strasbourg, Faculty of Medicine, Strasbourg, France*



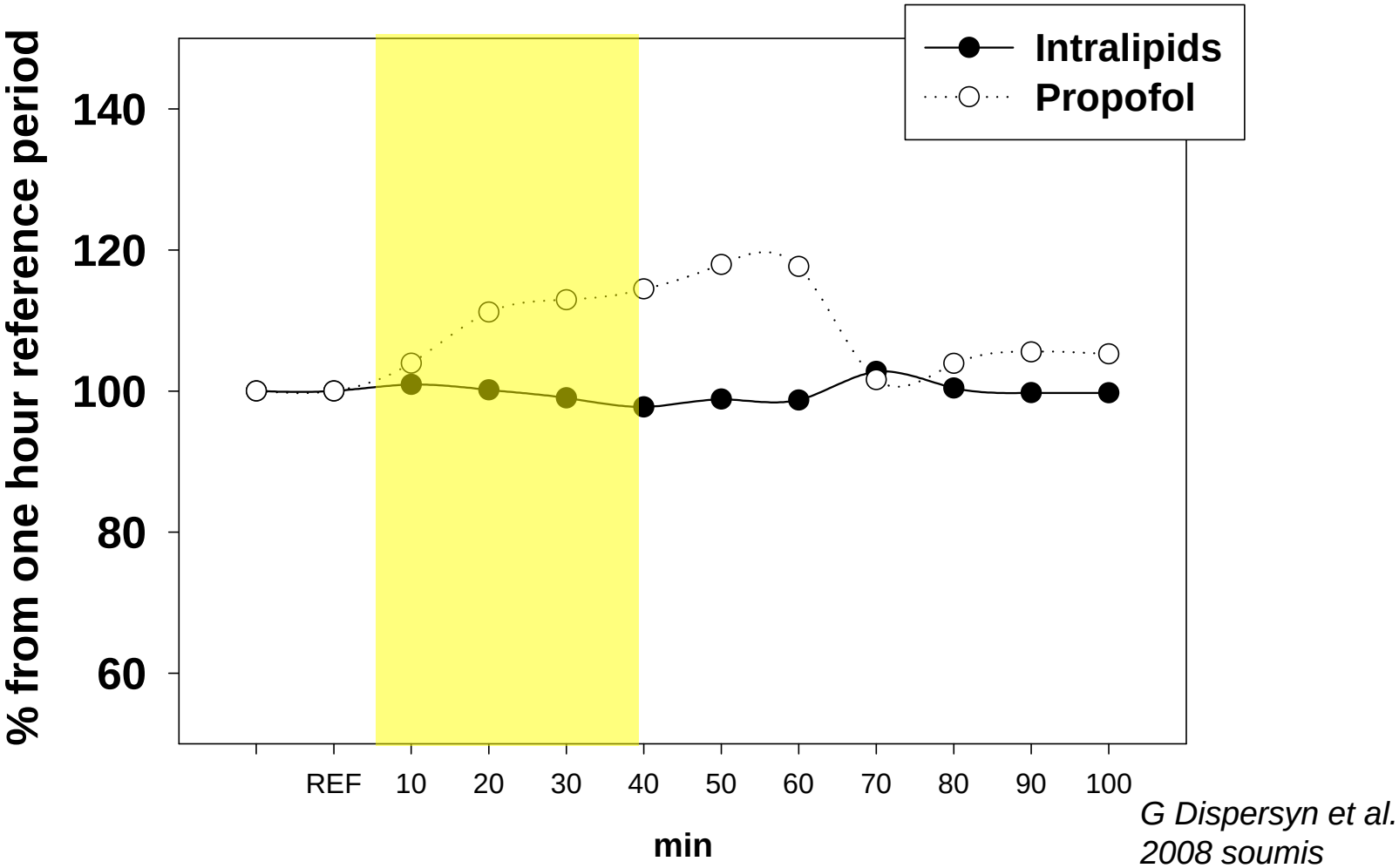


G Dispersyn et al.
2008 en cours de révision

anesthésie 20 minutes à CT16 (début d'activité CT12)



Périperfusion de glande pinéale isolée



G Dispersyn et al. 2008 soumis

J Anesth (2004) 18:228–231
DOI 10.1007/s00540-004-0249-1

Journal of
Anesthesia

© JSA 2004

Isoflurane increases, but sevoflurane decreases blood concentrations of melatonin in women

YOUNG-CHANG P. ARAI[1], WASA UEDA[2], YUJI OKATANI[3], TAKAO FUKAYA[3], and MASANOBU MANABE[1]

[1]Department of Anesthesiology, Kochi Medical School, Oko-cho, Nankoku 783-8505, Japan
[2]Departments of Anesthesiology, Clinical Physiology and Pharmacology, School of Nursing, Kochi Medical School, Nankoku, Japan
[3]Departments of Obstetrics and Gynecology, Kochi Medical School, Nankoku, Japan

t = 5 minutes

prémédication orale
benzodiazepine
1 heure avant !

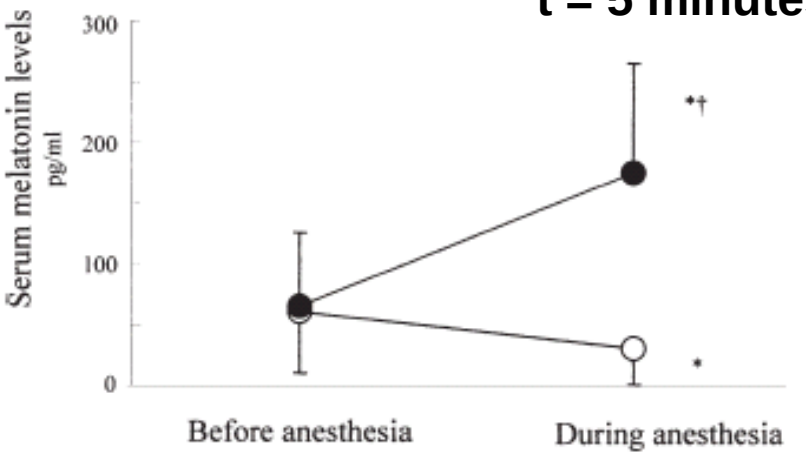


Fig. 1. Serum concentrations of melatonin before and during anesthesia in the isoflurane group I (ISO; *closed circles*), and the sevoflurane group (SEV; *open circles*). $*P < 0.05$ versus before anesthesia; $\dagger P < 0.05$ versus SEV group. Values for results are presented as means ± SD

Journal of Clinical Anesthesia (2007) 19, 120–124

ELSEVIER

Original contribution

No change in serum melatonin, or plasma β-endorphin levels after sevoflurane anesthesia☆

Argyro Fassoulaki MD, PhD, DEAA (Professor, Chairperson)[a,*],
Georgia Kostopanagiotou MD (Associate Professor)[a],
Pagona Meletiou (Pharmacist)[b],
Dimitris Chasiakos MD (Assistant Professor, Gynecologist)[c],
Sophia Markantonis PhD (Assistant Professor)[b]

Table 1 Melatonin (pg/mL) circulating levels before, immediately after anesthesia with sevoflurane, and two, 4, 8, and 24 hours after anesthesia; also in nonanesthetized healthy volunteers at the same time intervals

Melatonin	Before	End of anesthesia	2 h	4 h	8 h	24 h
Patients	n = 10	n = 13	n = 13	n = 13	n = 12	n = 13
Mean (SD)	8.2 ± 7.9	7.7 ± 7.9	7.1 ± 9.5	6.5 ± 6.1	7.8 ± 6.7	19.5 ± 17.9
CI	0.005-16.4	3.2-12.2	0.001-14.2	2.0-15.1	2.1-13.5	5.6-33.4
Volunteers	n = 13	n = 13	n = 13	n = 13	n = 13	n = 13
Mean (SD)	15.2 ± 15.0	11.1 ± 7.0	15.0 ± 11.8	15.6 ± 16.3	11.8 ± 9.9	23.7 ± 23.3
CI	7.8-22.3	7.2-15.0	8.7-21.2	8.1-23.1	6.8-10.8	11.5-35.9
Time effect	*df* = 3,09	F = 2.27	*P* = 0.088			
Group effect	*df* = 1	F = 4.18	*P* = 0.057			

CI = confidence interval.

Research Report

Circadian gene expression is suppressed during sevoflurane anesthesia and the suppression persists after awakening

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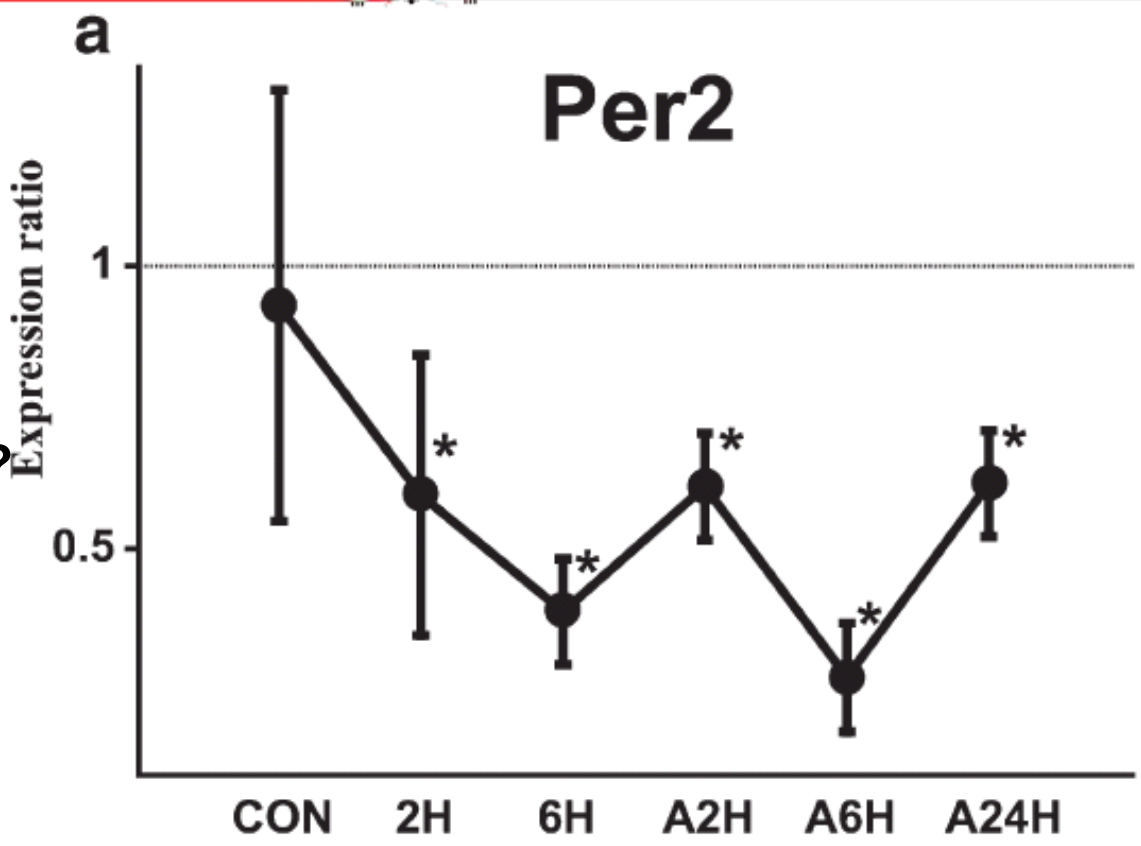
whole brain rat
sevoflurane 4%
2 h or 4 h
(n=9/group)

hour of anesthesia ?



Halogénés

- hypothèse : probable effet sur horloge interne
- à tester sur modèle animal
- conséquences chez l’enfan
- mécanisme ?

‘Merci … de votre attention