

La mitochondrie

Source d'énergie

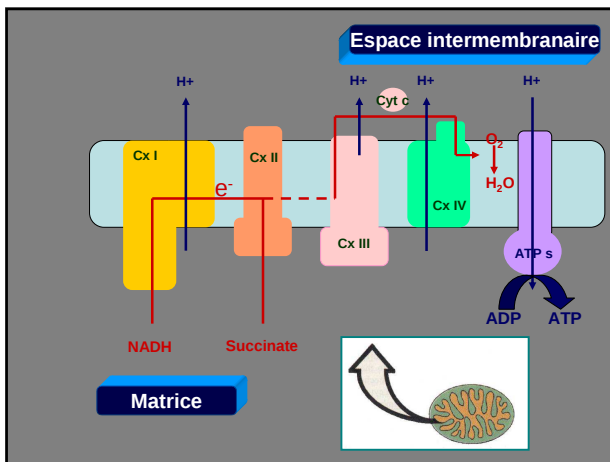
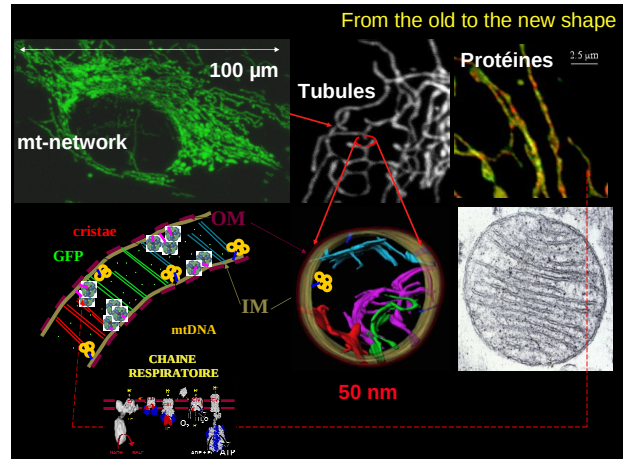


Transformation

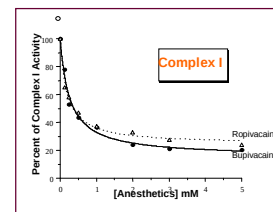


MITOCHONDRIA

Consommation



Inhibition du Cx I de la chaîne respiratoire



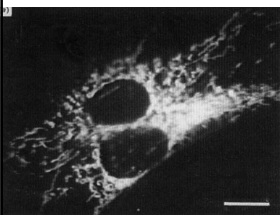
	Complex I	Complex II	Complex III	Complex IV
Control	358 ± 15	497 ± 26	1346 ± 80	4350 ± 335
Bupivacaine 5 mM	73 ± 8*	406 ± 18*	1297 ± 78	4109 ± 408

Sztark F. Anesthesiology 1998; 88 :1340-9

Suppression du $\Delta\Psi$ in situ par la bupivacaine

Dépolarisation de la membrane mitochondriale

Fibroblaste



Grouselle P. Biochem J 1990; (277)14 :

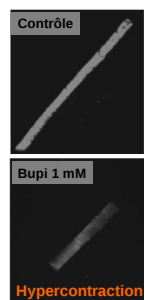


Bupivacaine myotoxicity is mediated by mitochondria

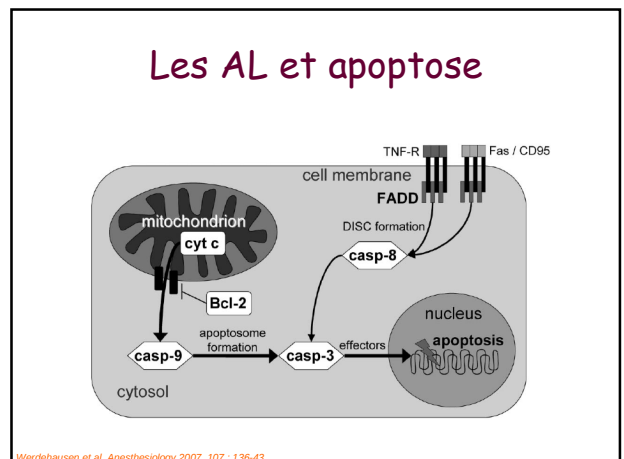
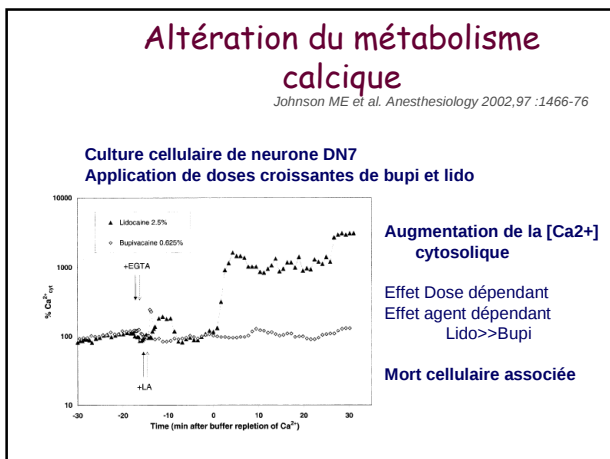
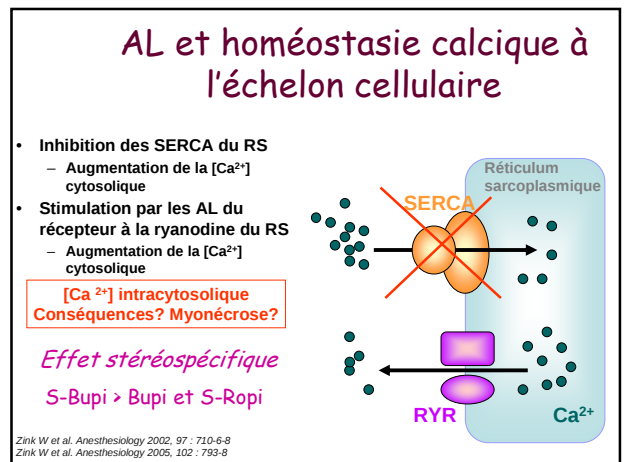
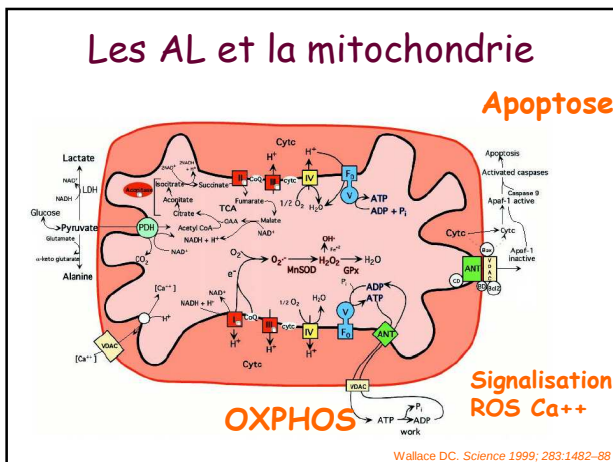
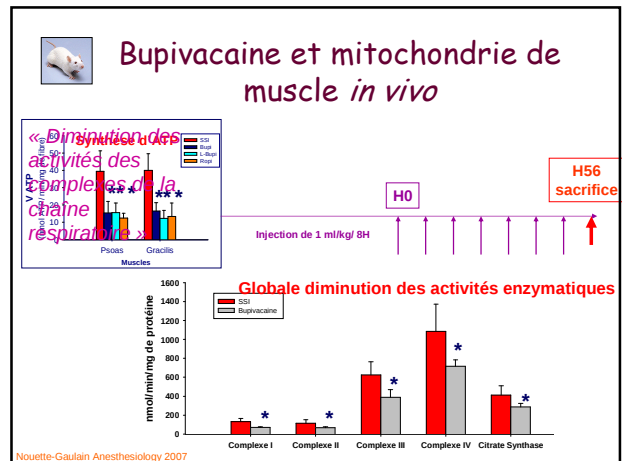
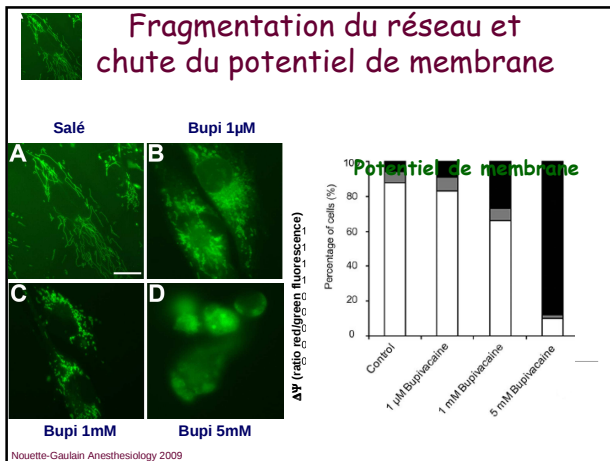
Altérations des oxydations phosphorylantes

- Inhibition du complexe I
- Effet « uncoupler »
- Altération du potentiel redox
- Altération du potentiel de membrane

Diminution de la synthèse d'ATP
Myonécrose



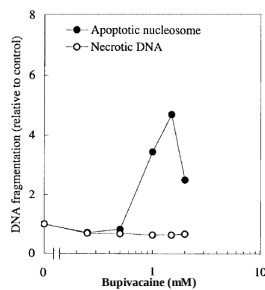
Irwin W et al. JBC 2002;277:12221-7



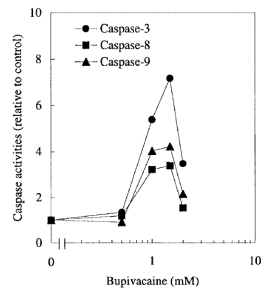
Bupivacaine et apoptose

Cellules HL60

Fragmentation de l'ADN

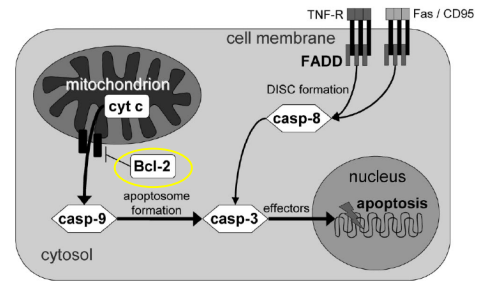


Activation des caspases



Unami et al. Journal of Toxicological Sciences 2003, 107 : 79-94

Lidocaïne et apoptose

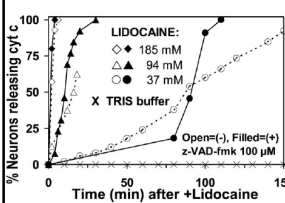


Werdehausen et al. Anesthesiology 2007, 107 : 136-43

Lidocaïne et apoptose

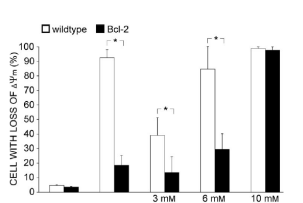
Lidocaïne libération de cytochrome c **Bcl-2** protège de la perte du $\Delta\Psi$

ND7 Cell line



Johnson 2004 Anesthesiology

Jurkat cells wild type, Bcl-2+ ou Casp-9-

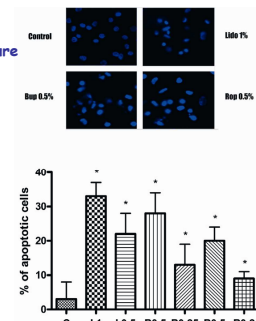


Werdehausen et al. Anesthesiology 2007, 107 : 136-43

JBJS Apoptosis and Mitochondrial Dysfunction in Human Chondrocytes Following Exposure to Lidocaine, Bupivacaine, and Ropivacaine

By Valentina Grishko, PhD, Min Xu, MD, Glenn Wilson, PhD, and Albert W. Pearall IV, MD
J Bone Joint Surg Am. 2010;92:609-18

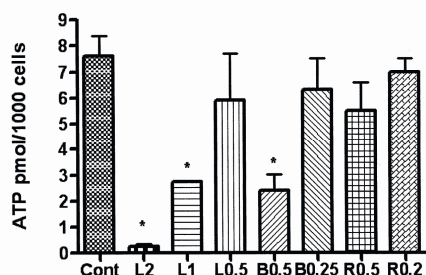
Apoptose 120Heures
Après une exposition d'une heure



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Apoptose et synthèse d'ATP



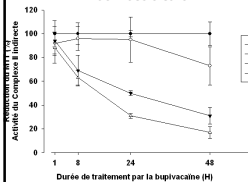
Facteurs de risque?
Agents protecteurs?

Effet temps et effet concentration

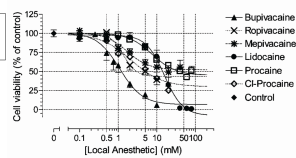
*Lésions plus sévères avec
-le temps
-les concentrations croissantes*



Culture cellulaire
de **myoblastes**
humains issu
de muscle strié



Culture cellulaire
de **neurones**
humains



Nouette-Gaulain Anesthesiology 2009

Perez Castro Anesth Analg 2009

Effect of bupivacaine on intervertebral disc cell viability

Ho Lee, MD, PhD^{1,2}, Gwendolyn Sowa, MD, PhD^{1,3,4}, Nam Vo, PhD¹, Gianluca Vadala, MD¹,
Stephen O'Connell, DO¹, Rebecca Studer, PhD^{1,5}, James Kang, MD¹

The Spine Journal 10 (2010) 159–166

Effet temps et concentrations

