



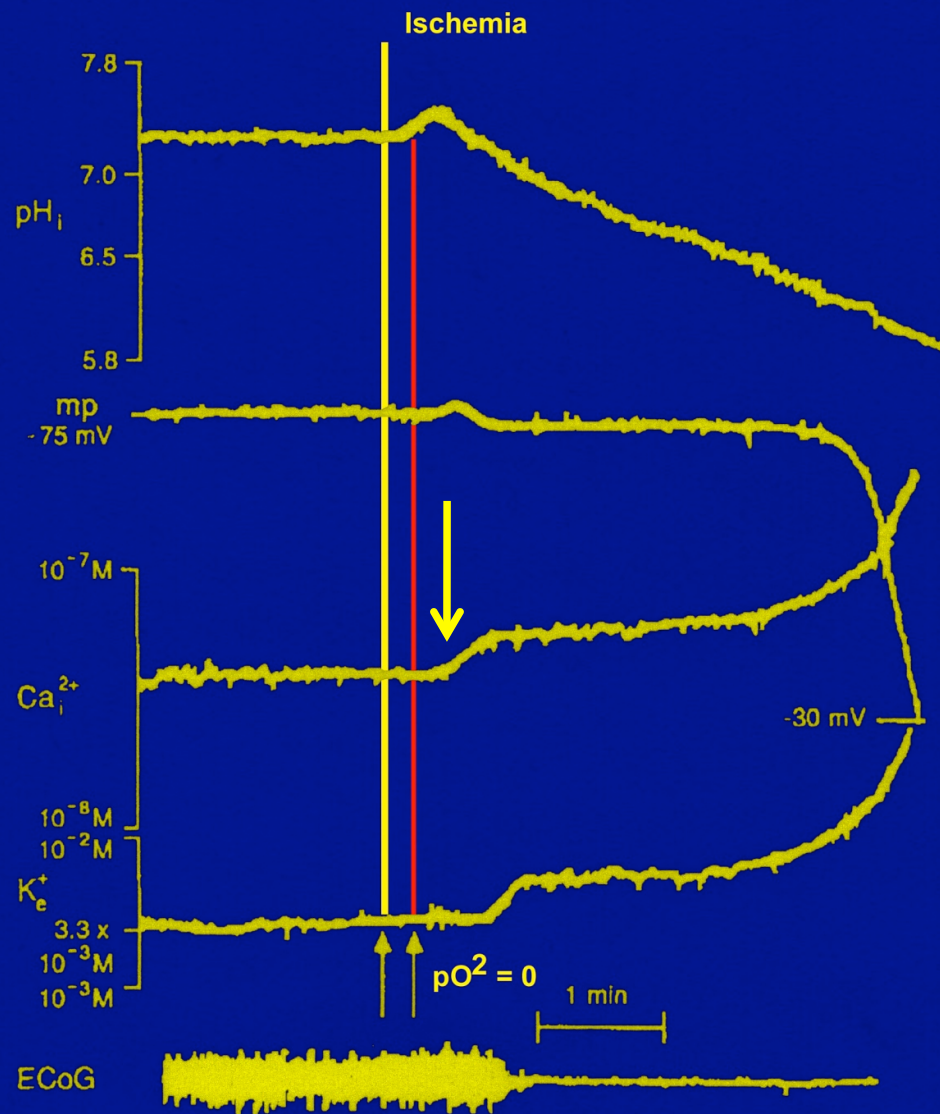
Calcium - mitochondria pipeline hypothesis and neuronal tissue sensitivity to ischemia



Gemeinsame Jahrestagung 2009
SGN
St Gallen
Ph Bijlenga



Acute neuronal tissue response to anoxia



Intracellular [Calcium] increase

Acidification

Loss of activity

Cellular depolarisation

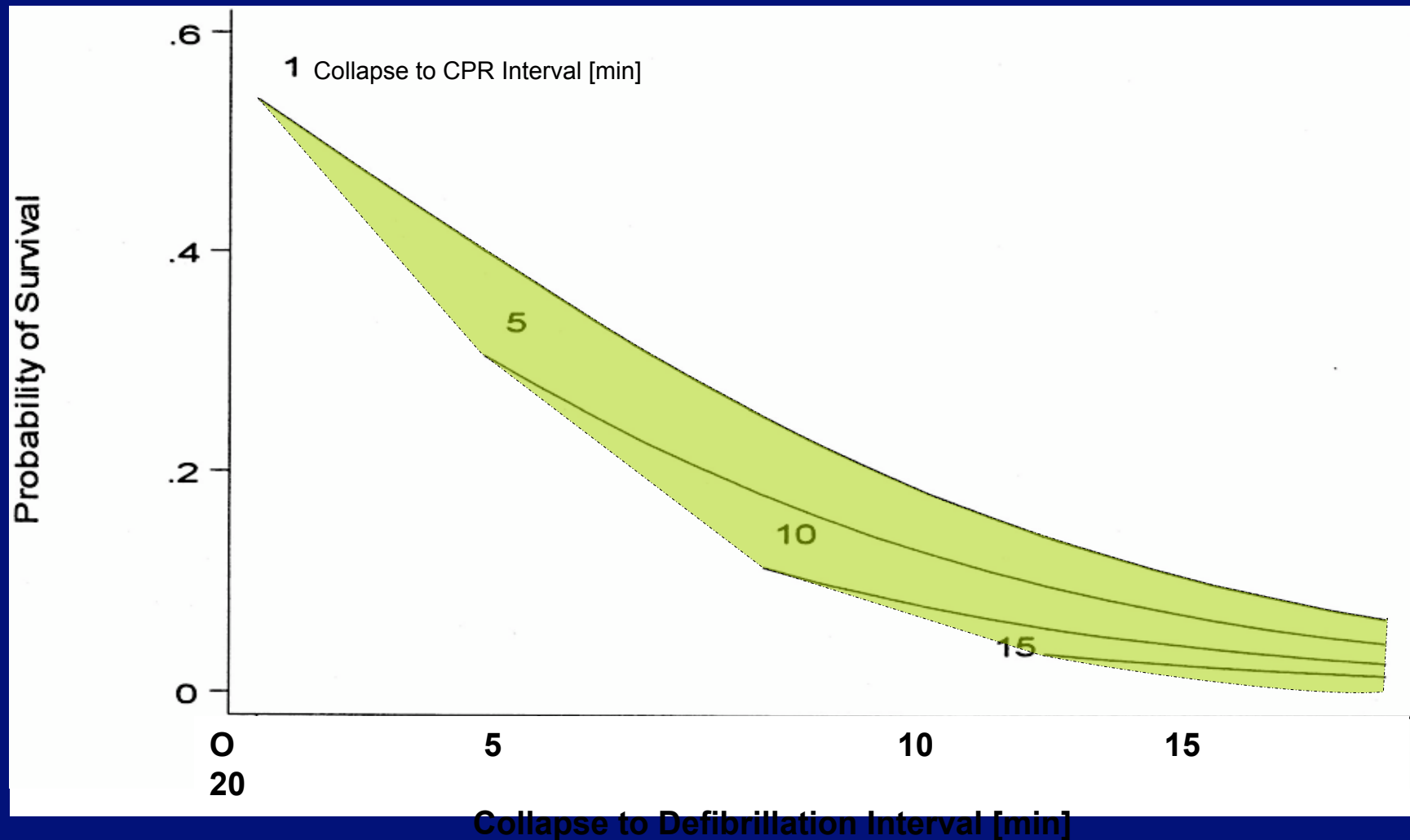
Exitotoxicity

Silver & Erecinska J Gen Physiol 1990



© BBC November 2002
Horizon - Freak Waves

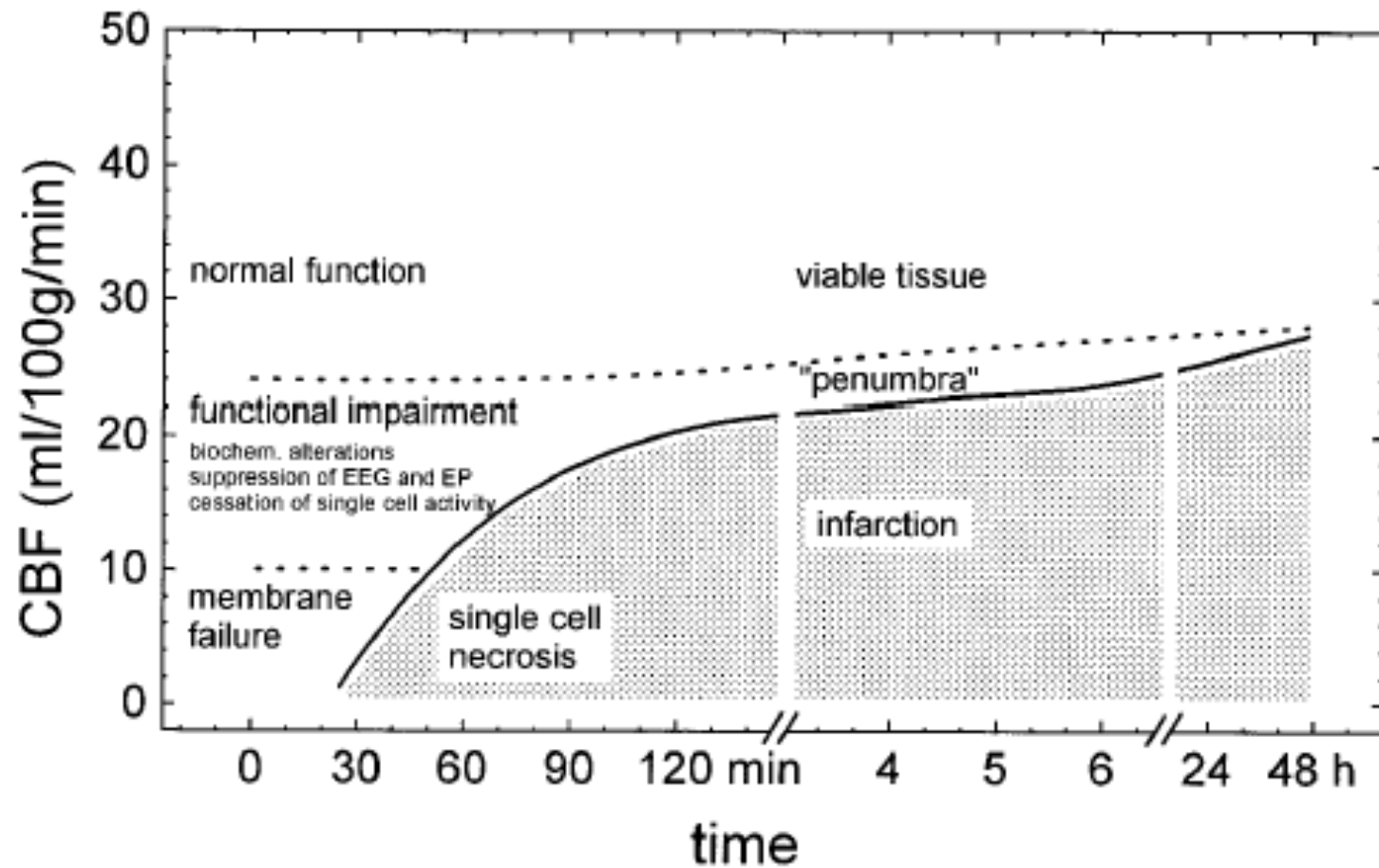
Cardiac Arrest – Effect of CPR



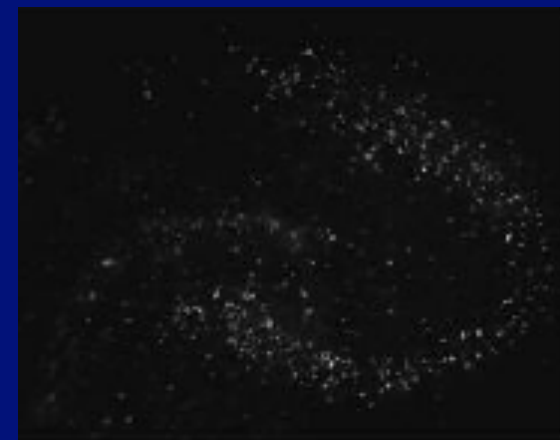
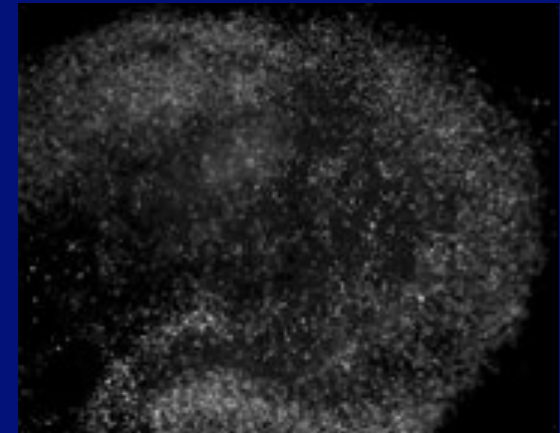
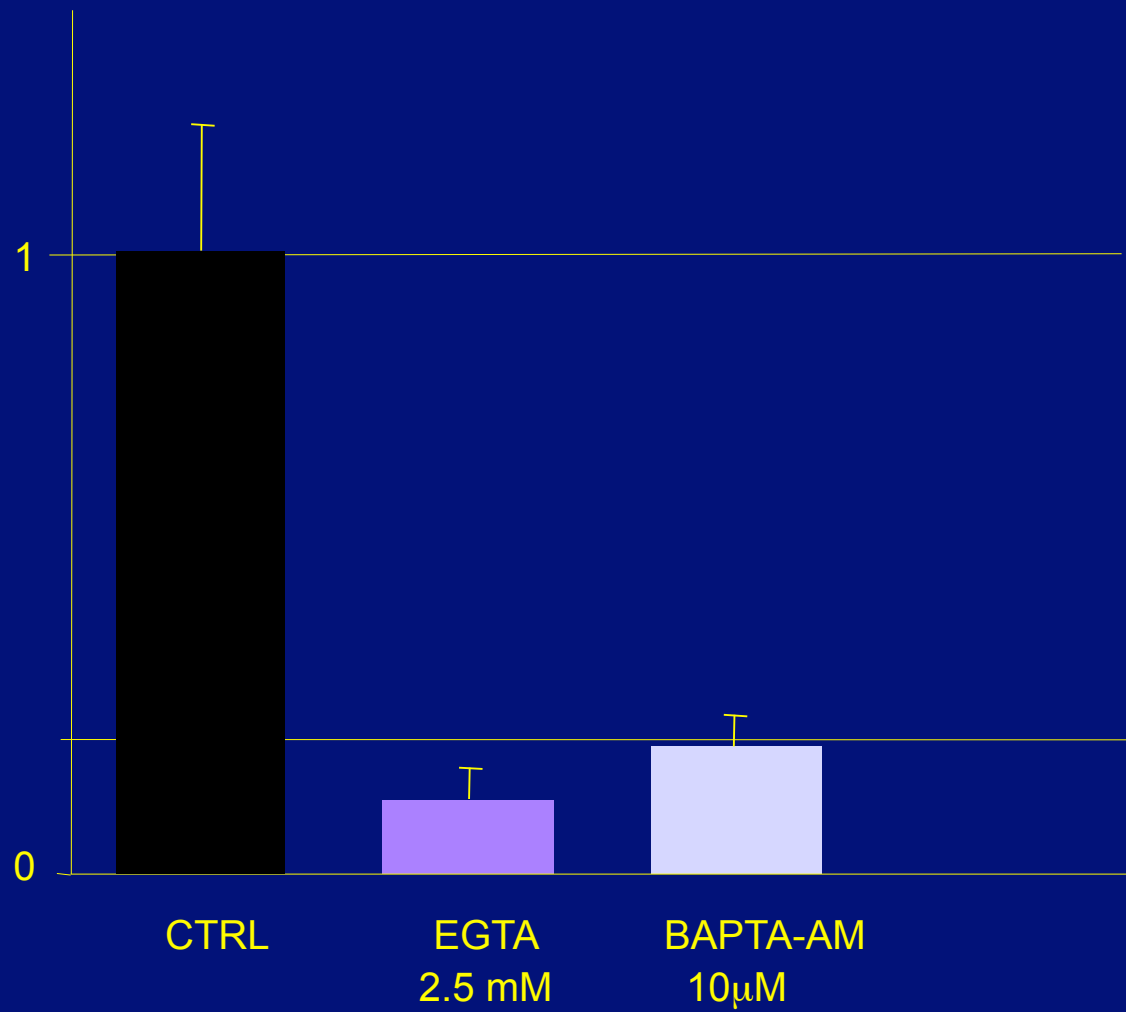
Valezuela et al. Circulation 1997

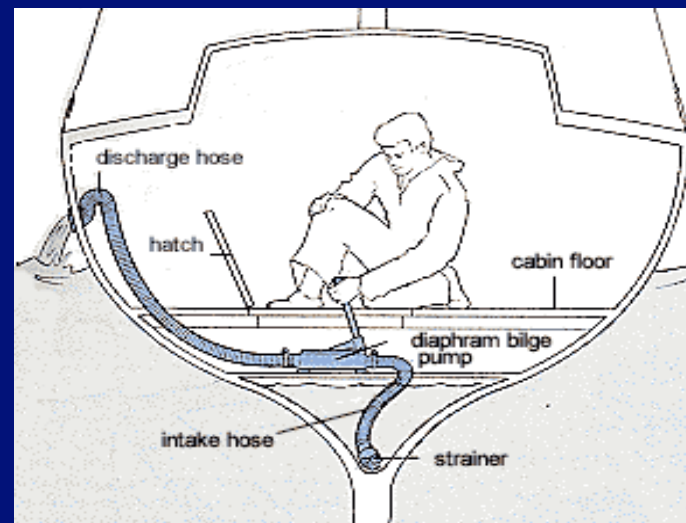


Ischemia



Calcium flooding





Why did all anti-calcic treatment fail ?

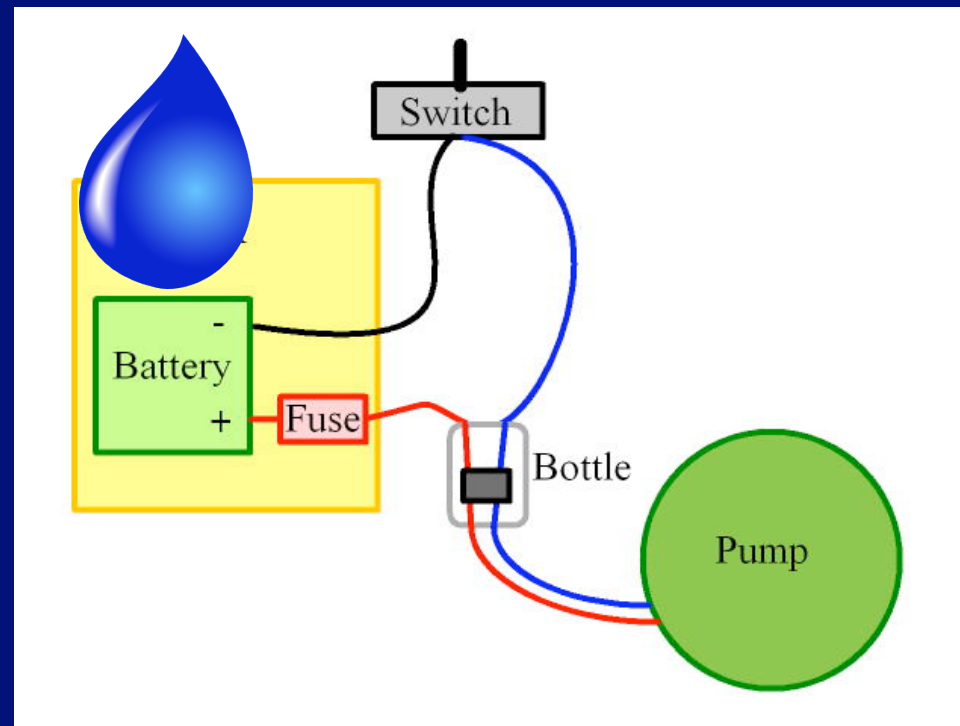
Barbiturate

Ketamine

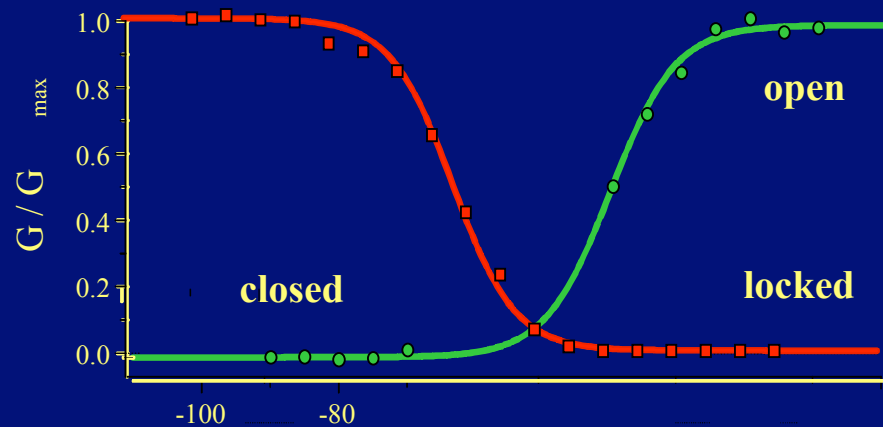
Calcium channels inhibitors

Why did all anti-calcic treatment fail ?

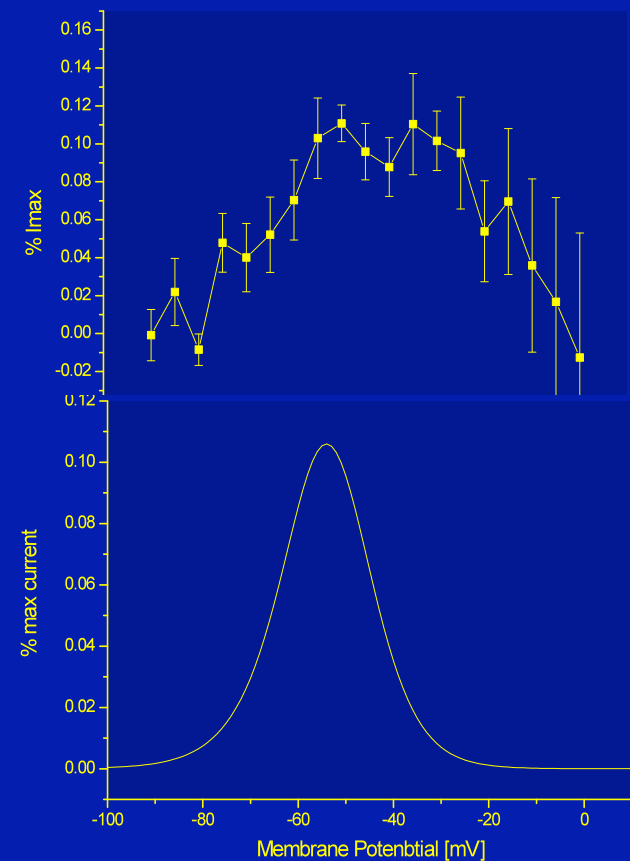
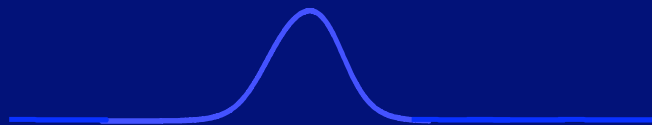
Water



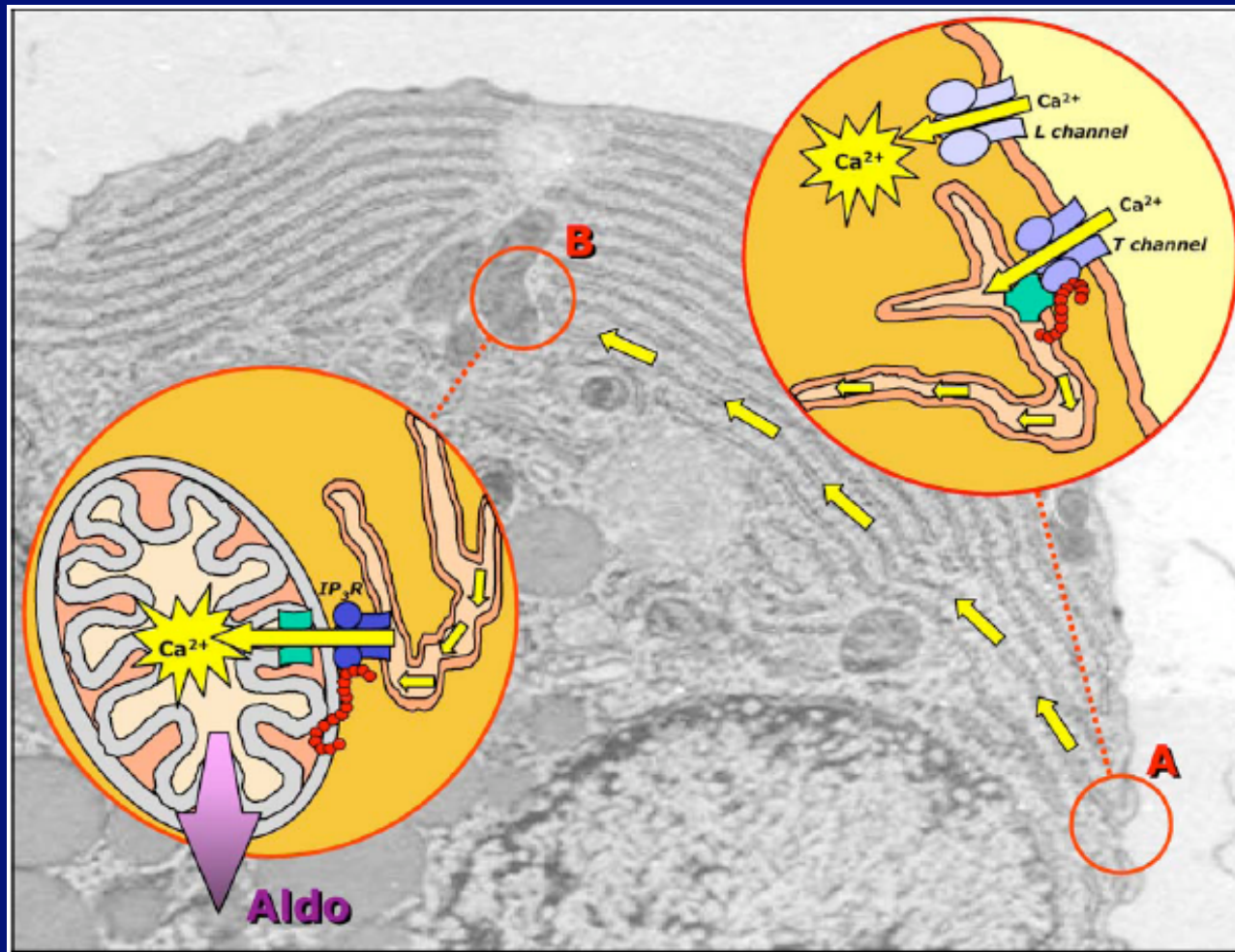
T-type biophysical properties



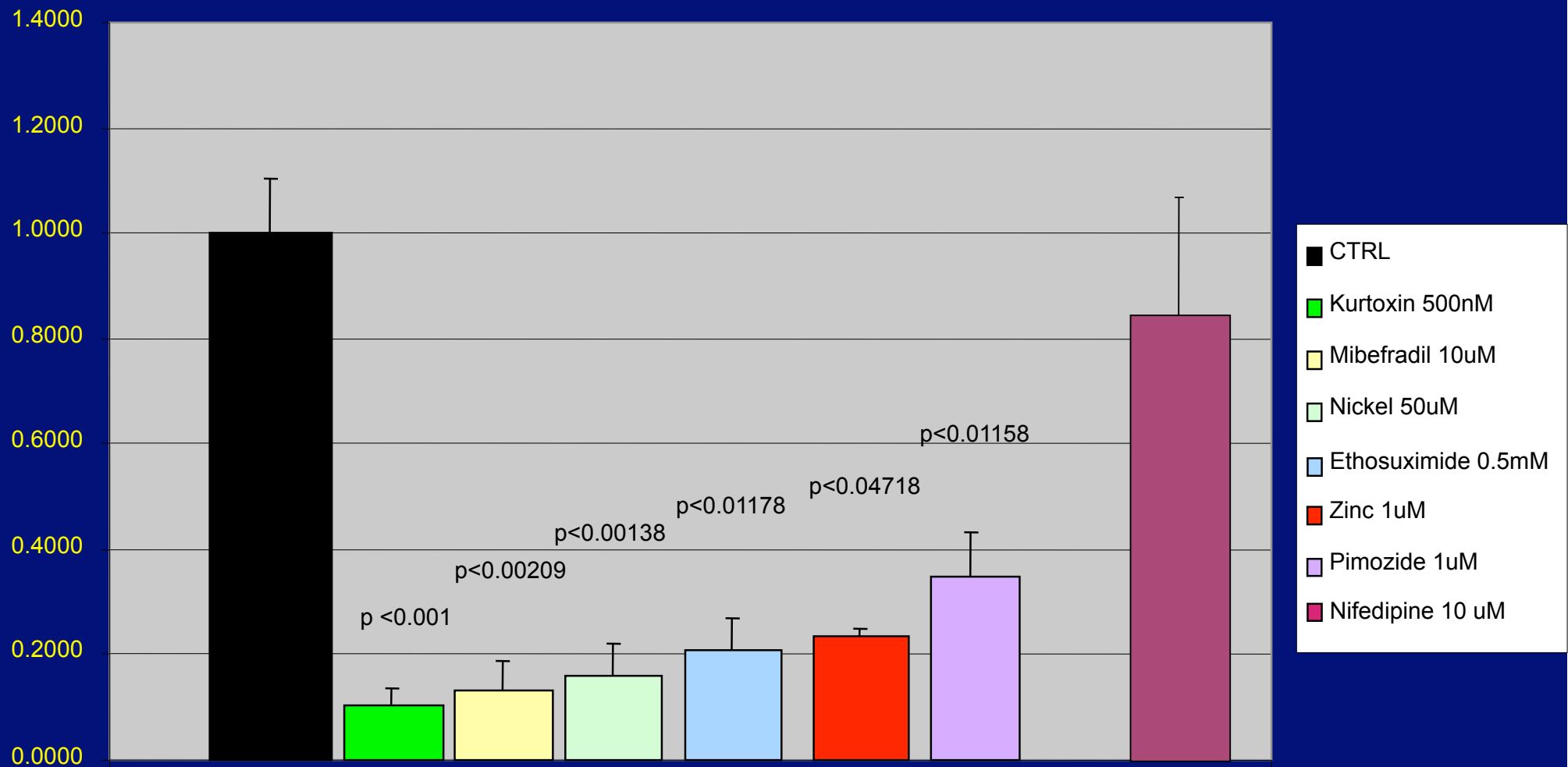
Window current



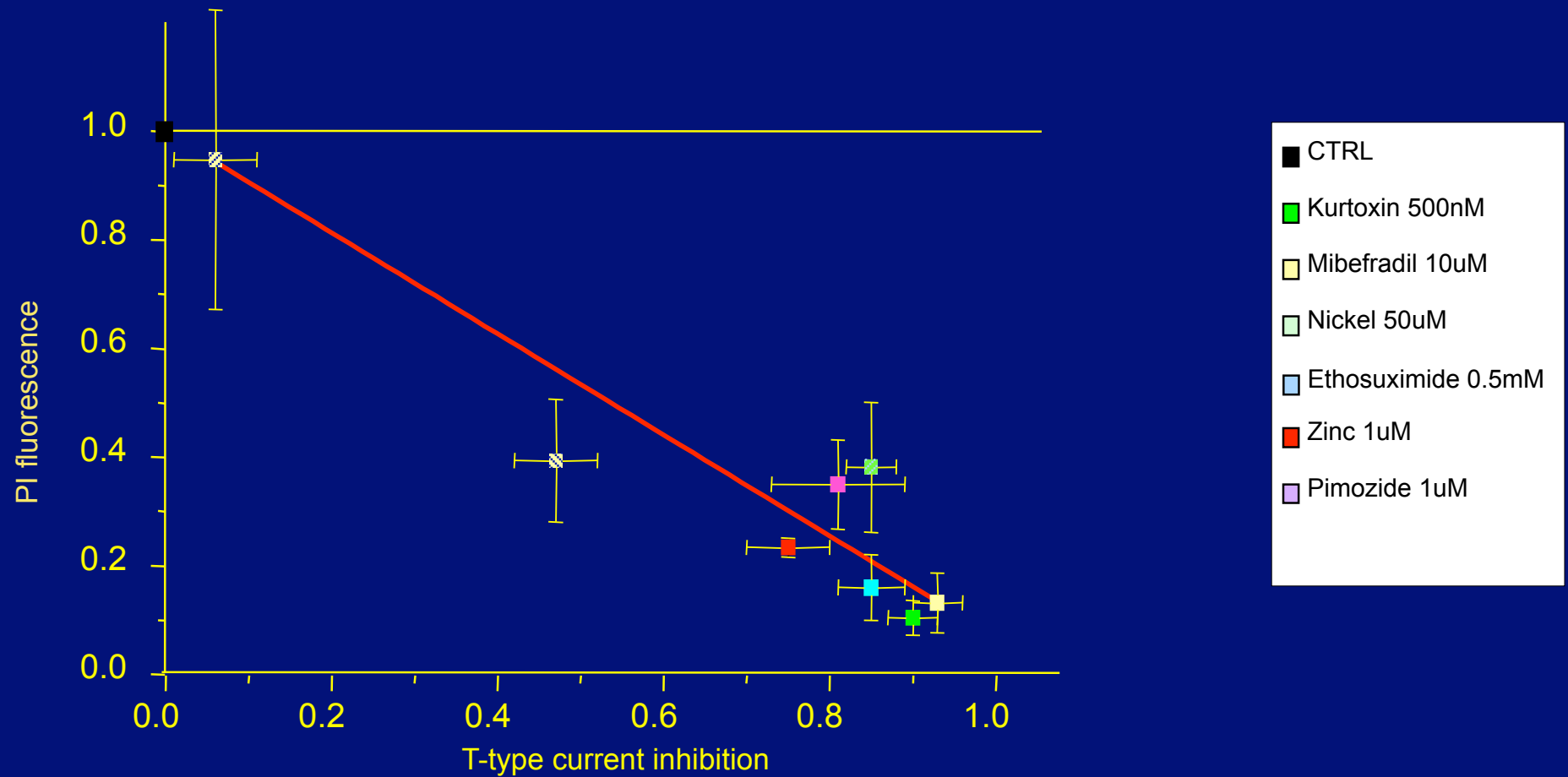
Pipeline hypothesis



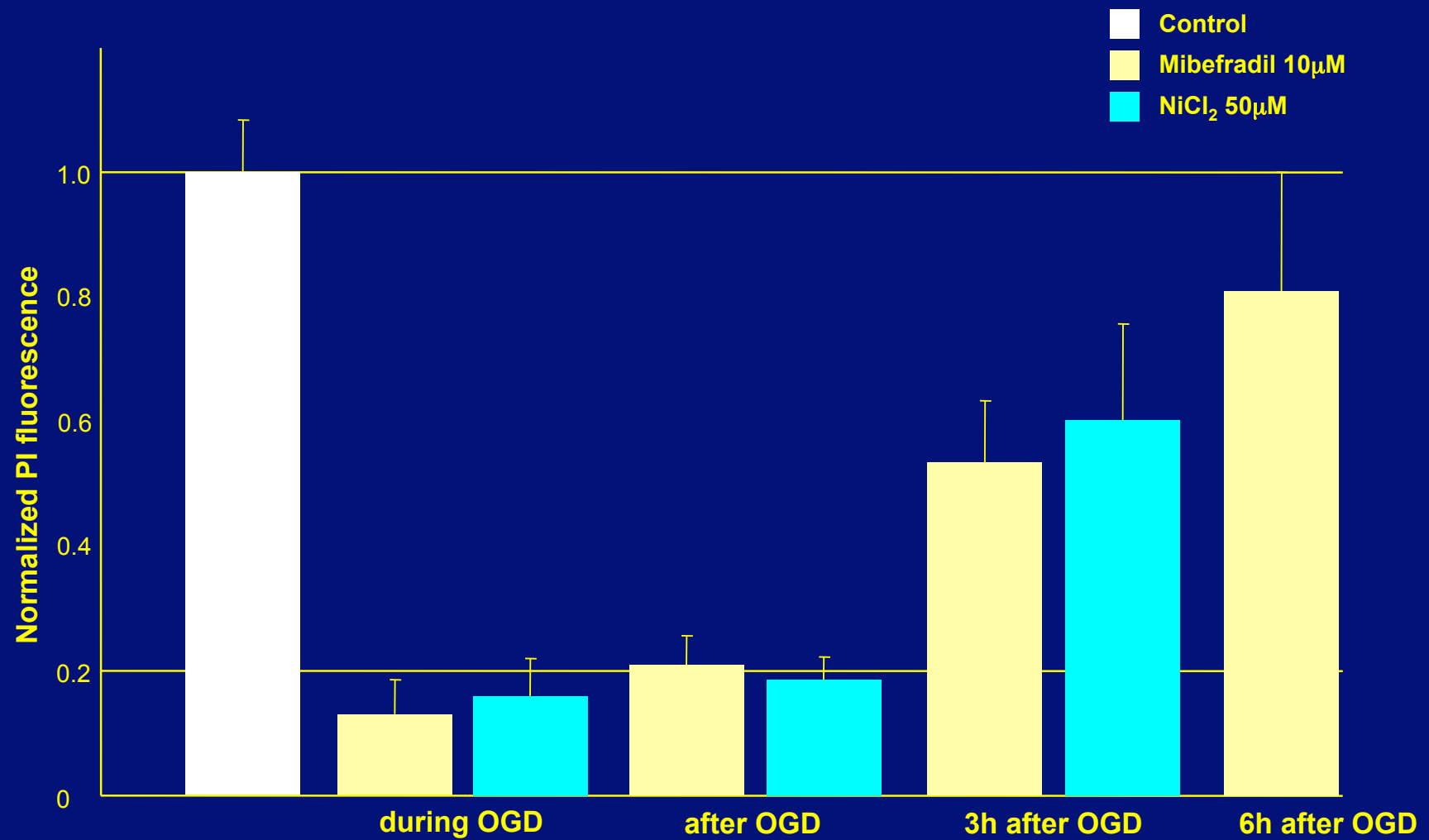
Inhibition of T-type calcium channels during ischemia protects neurones from delayed death.



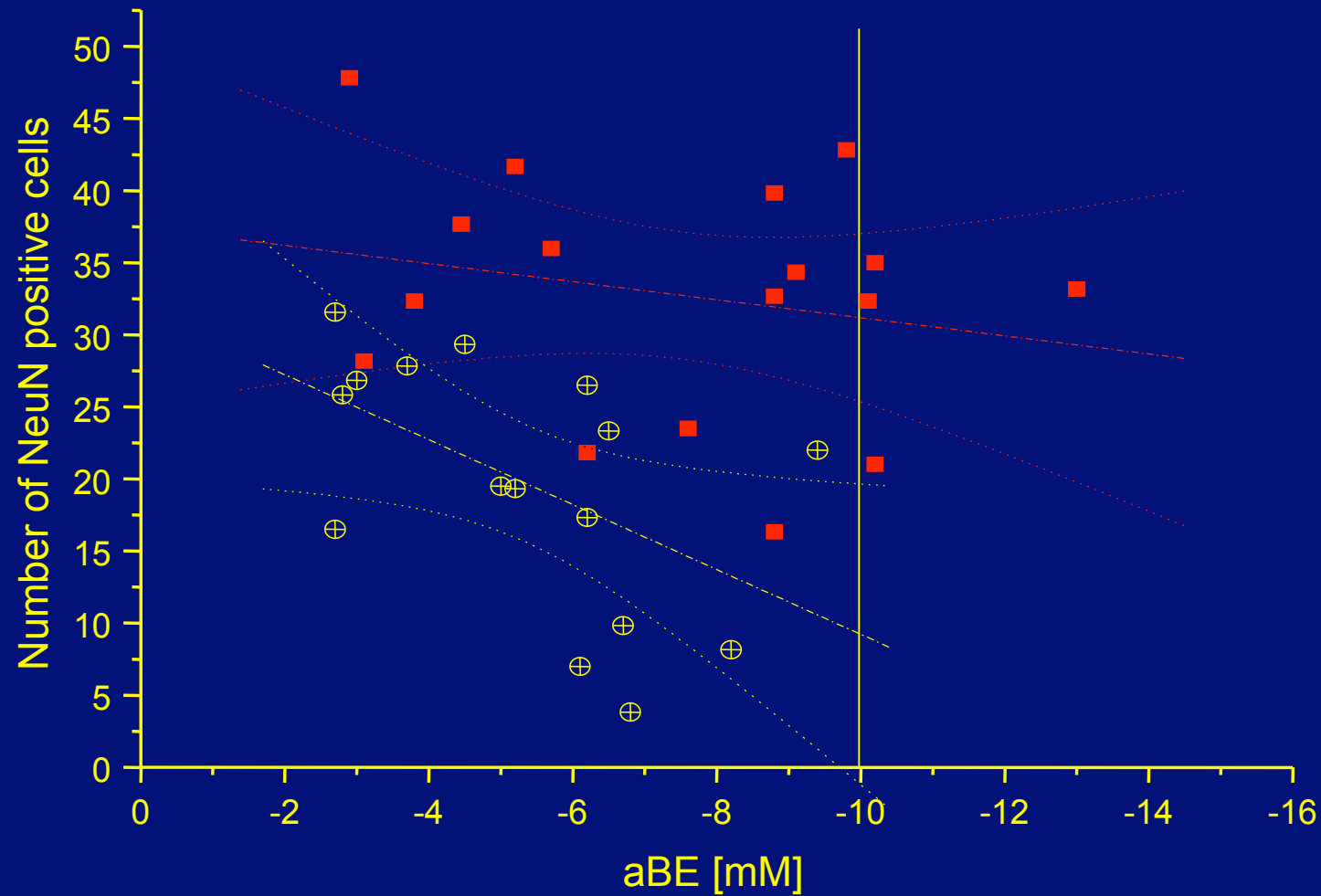
Cell death decreases with T-type current inhibition



Treatment is effective even if applied after insult



**The effect is reproduced *in vivo*
in a rat model of global ischemia**



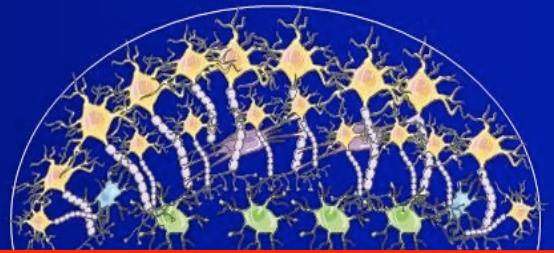
Mortality of animals subject to severe ischemia is reduced by treatment

Severe ischemia
aBE < -10

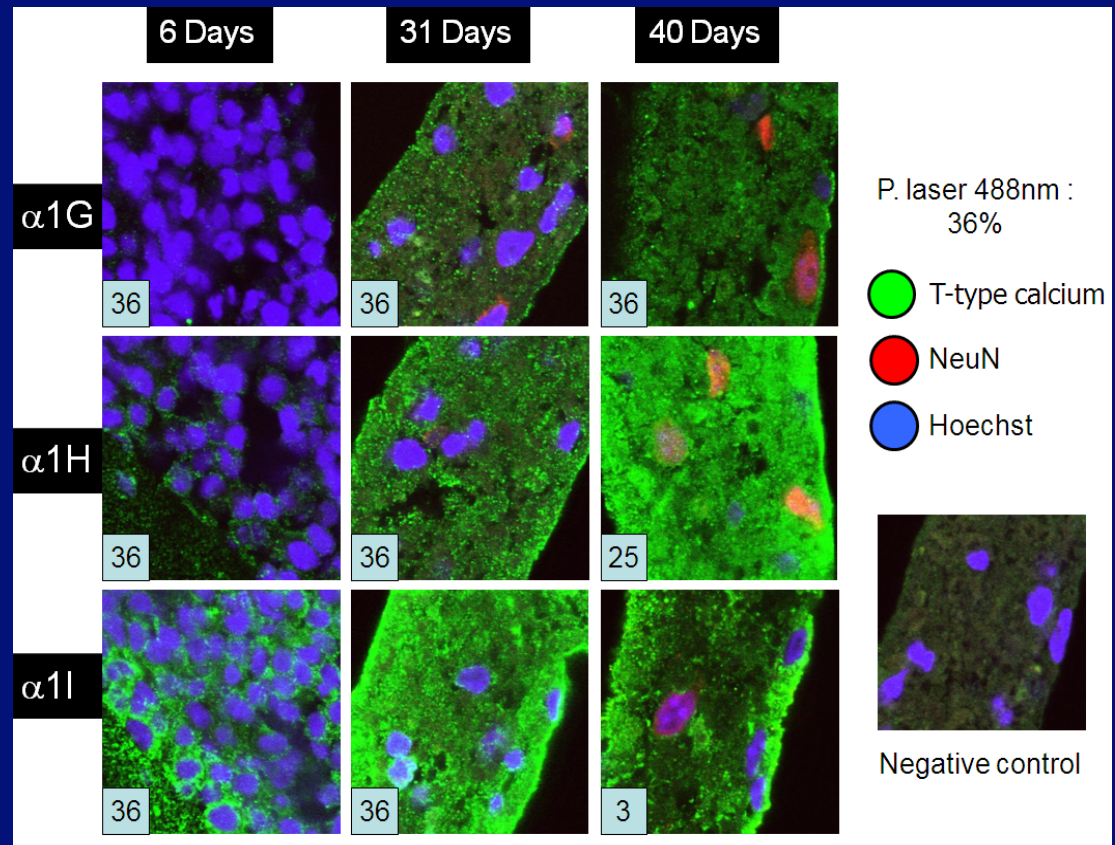
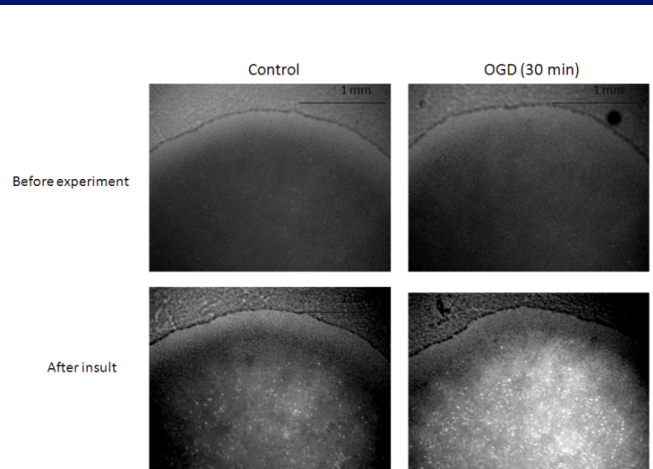
	P	T
😊	0	4
☠️	5	1

$p = 0.047$

Calcium signaling during ischemia



Medium MEM HS 25%



Thanks to:

- Yves Gouriou
- Irina Nikonenko
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- Nicolas Demaurex
- Carlo Schaller

