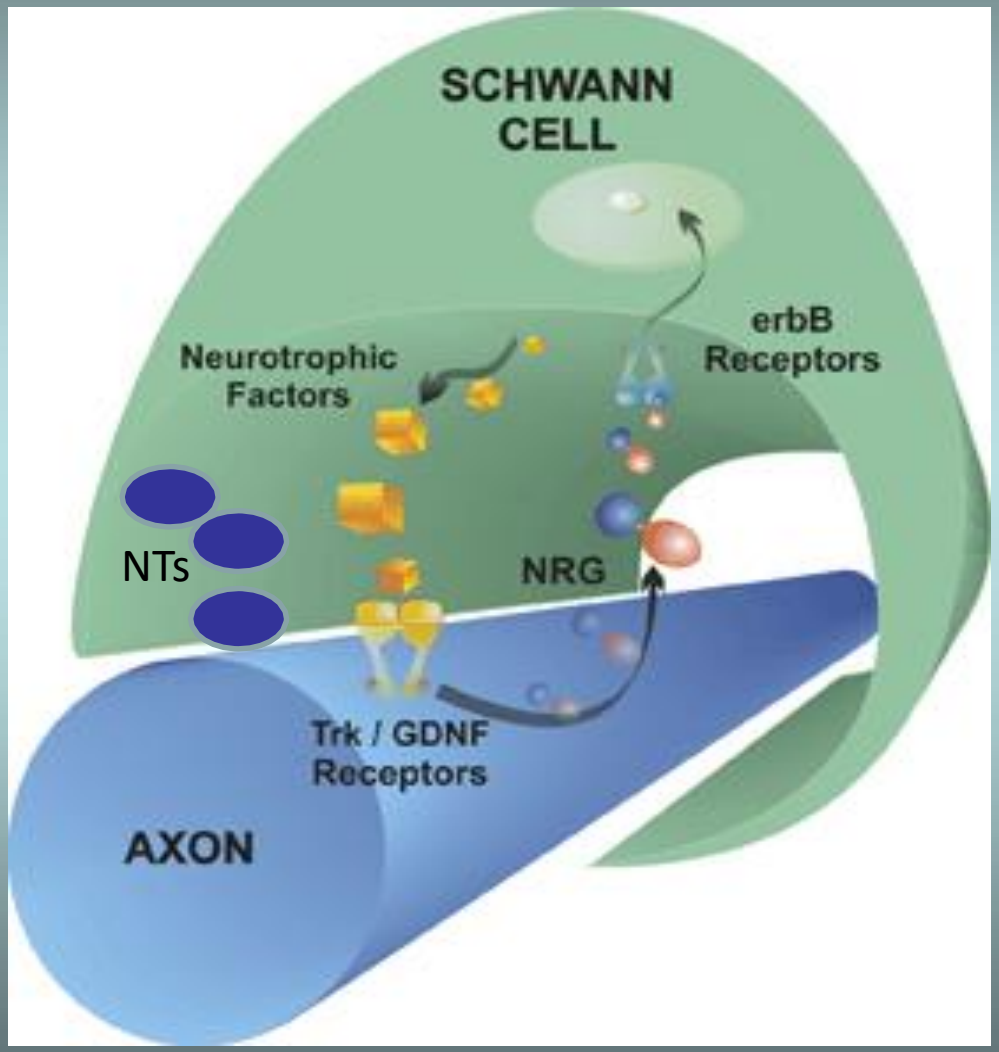
Interazione neurone-glia 2

Ruoli alternativi dei neurotrasmettitori



Neurotransmitters as growth regulatory signals: role of receptors and second messengers

Lauder JM, Trends . 1993 Jun;16(6):233-240

- A number of 'classical' neurotransmitters are present in primitive organisms and early embryos in the absence of a nervous system, and pharmacological evidence indicate that these substances regulate morphogenetic activities such as proliferation, differentiation, cell motility and metamorphosis.
- The chemical mediators signals of neurotransmitters may be evolved from more primitive functions in lower organisms where these substances were used as both intra- and intercellular signalling devices.
- These phylogenetical old functions may be reiterated in the developing nervous system and in the humoral functions of neurotransmitters outside the nervous system.

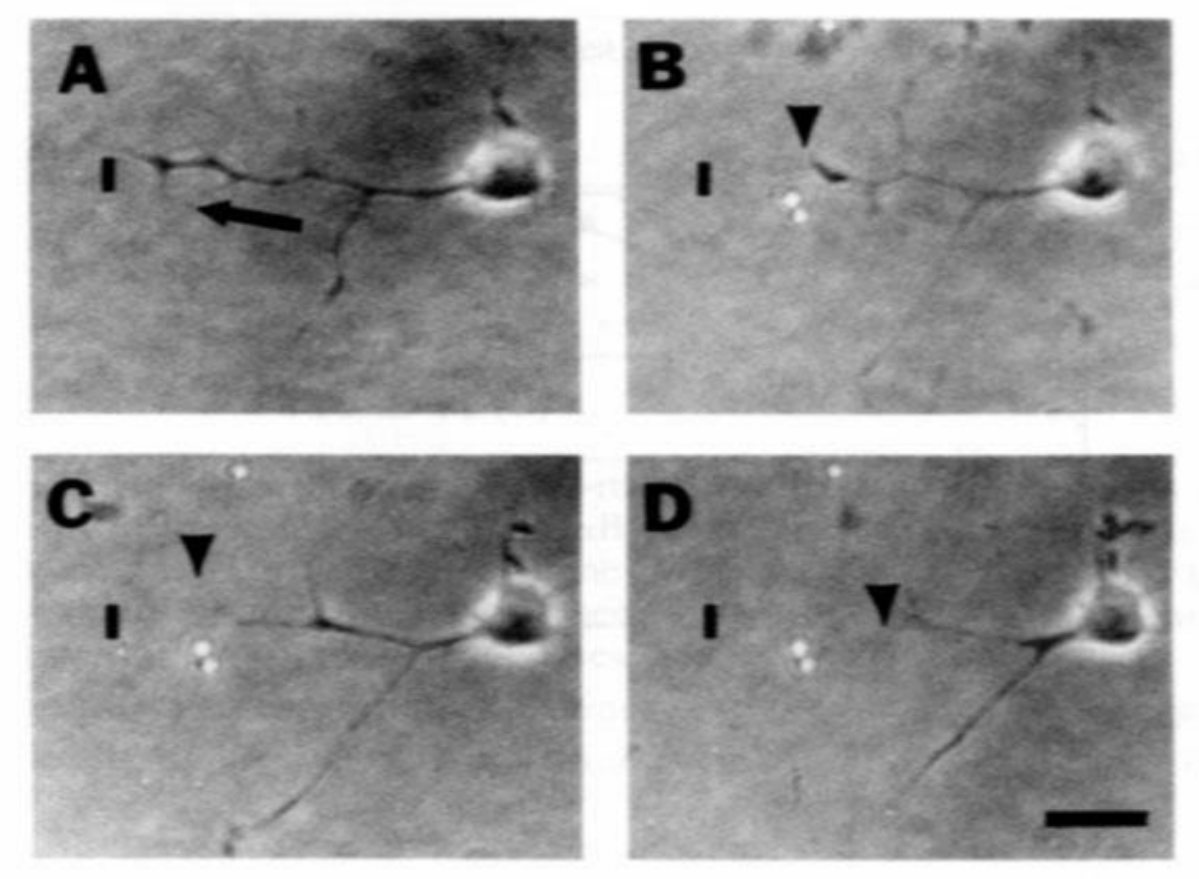
Neurotrasmettitori durante la neurogenesi

I neurotrasmettitori e i loro recettori vengono espressi precocemente durante lo sviluppo del SN

Effects of neurotransmitters on neurite outgrowth, plasticity and survival

Neurotransmitter	Neuronal preparation	Effect
Acetylcholine	Rat retinal ganglion cells	Inhibits neurite outgrowth
	Chick retina	Inhibits neurite outgrowth
	Hippocampus	Inhibits dendrite outgrowth
	Adult *Helisoma*	Prevents inhibition of outgrowth by serotonin
Dopamine	Chick retina	Inhibits neurite outgrowth
	Helisoma	Inhibits neurite outgrowth
	Rat striatum	Prerequisite for ischemic injury
GABA	Rat hippocampus	Prevents glutamate-induced dendrite regression
Glutamate	*Helisoma*	Promotes neurite sprouting
	Rat hippocampus	Promotes dendritic regression, low dose (AMPA)
	Rat hippocampus	Promotes neurite sprouting (NMDA)
	Rat hippocampus	Produces cell death (high dose)
	Mouse cortex	Produces cell death (high dose)
	Rat retinal ganglion cells	Produces cell death (high dose)
	Tadpole optic tectum	Stabilizes co-active visual synapses (NMDA)
Norepinephrine	Rat cortex	Produces cell death
Serotonin	*Helisoma*	Inhibits neurite outgrowth
Somatostatin	Adult *Helisoma*	Promotes neurite sprouting
VIP	Mouse spinal cord	Prevents cell death produced by electrical blockade
	Rat retinal ganglion cells	Prevents cell death produced by electrical blockade

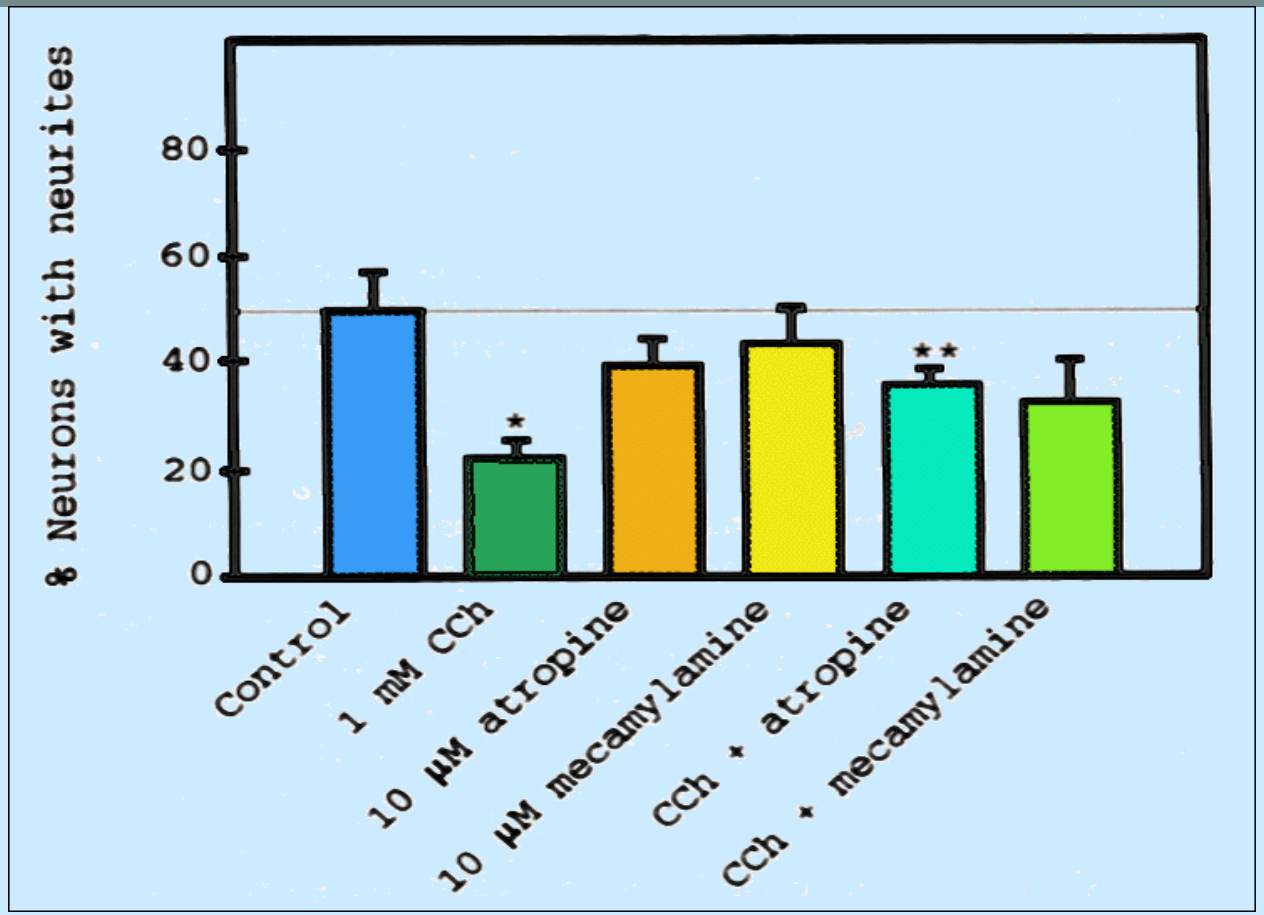
Nicotine Induces Neurite Retraction in Ciliary Ganglion Neurons from Chick Embryos



La via nicotinica inibisce la crescita neuritica in neuroni di gangli ciliari di embrioni di pollo

Pugh and Berg, J. Neurosci. 14: 889-896; 1994

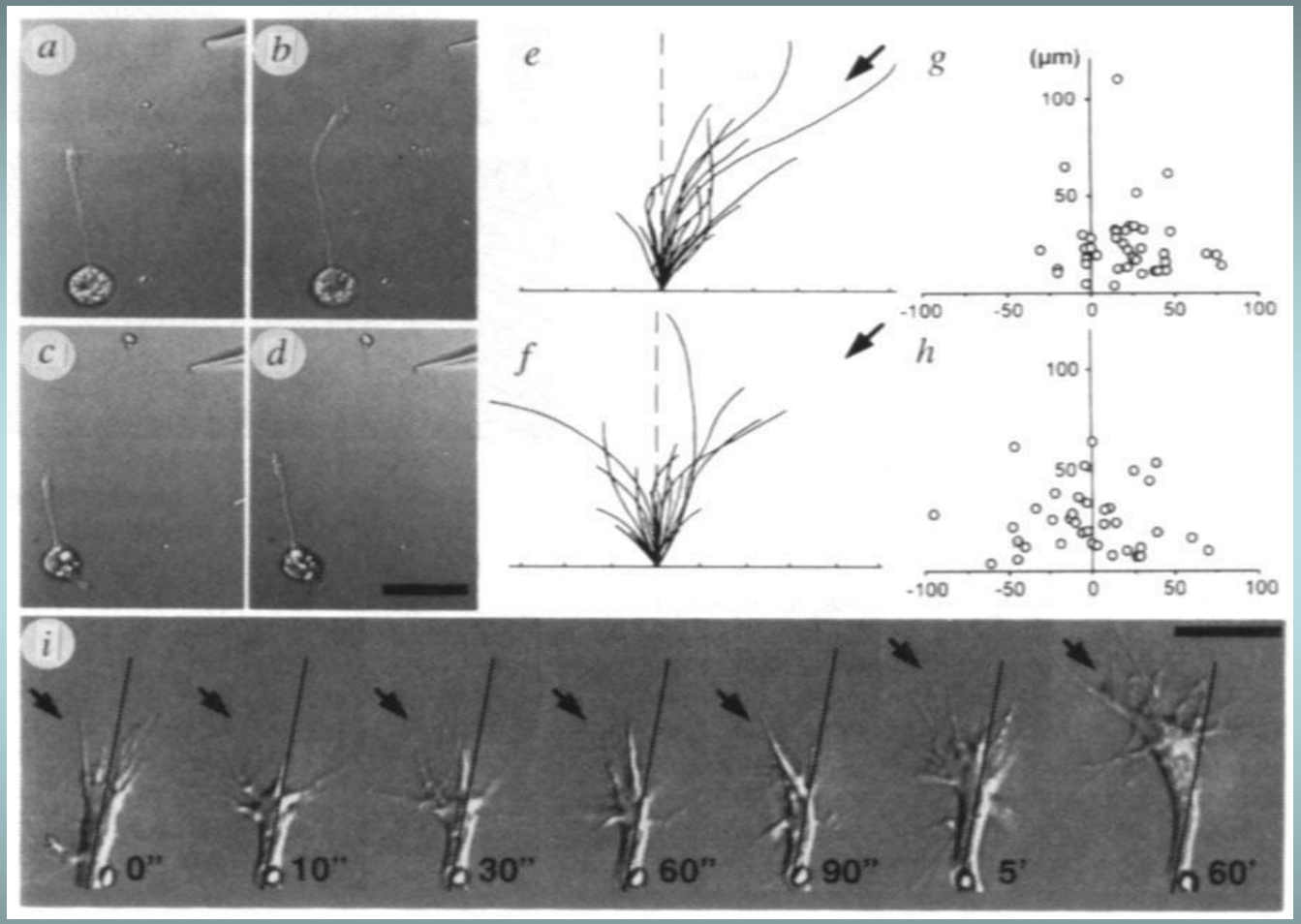
Effect of CCh and Cholinergic Receptor Antagonists on Neurite Outgrowth from Isolated Chick Sympathetic Neurons



La via muscarinica inibisce la crescita neuritica nei neuroni di gangli simpatici di pollo

Small et al., J. Neurosci. 15: 144-151; 1995

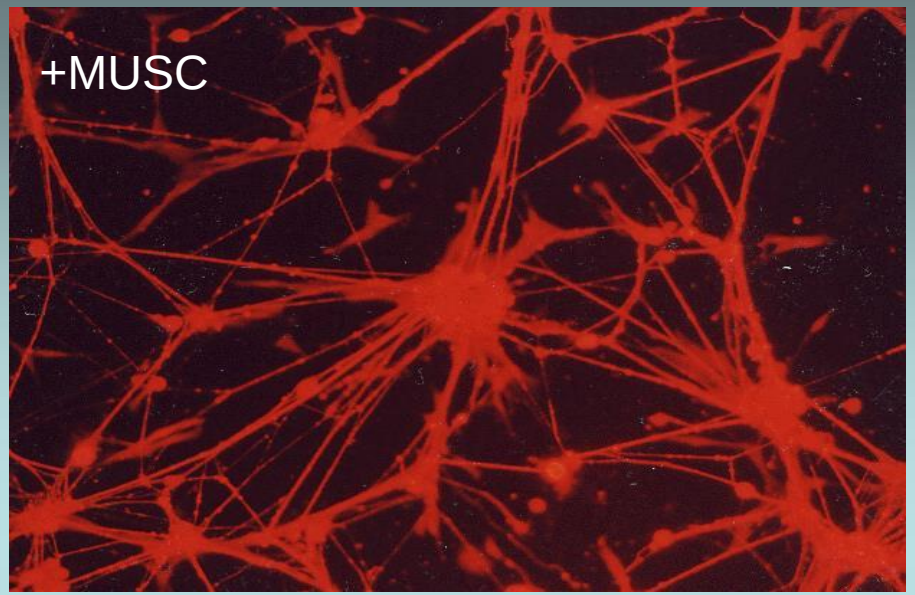
Turning Response of *Xenopus* Spinal Neuron in the Presence of ACh Gradient

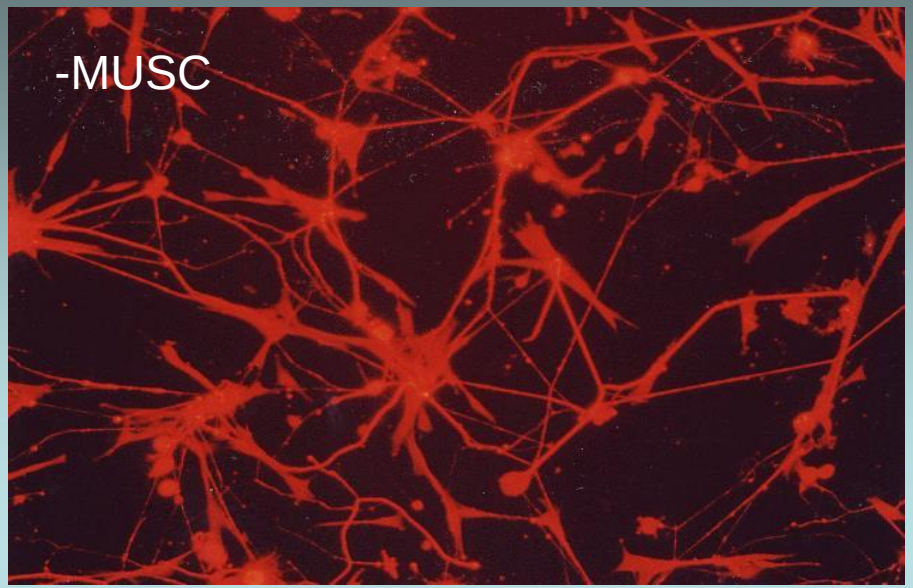


La via colinergica ha un effetto chemioattraente per i neuriti in crescita di neuroni spinali di Xenopus

Zheng et al., Nature 368: 140-144; 1994

ACh stimola la crescita neuritica nei neuroni sensoriali di embrioni di pollo

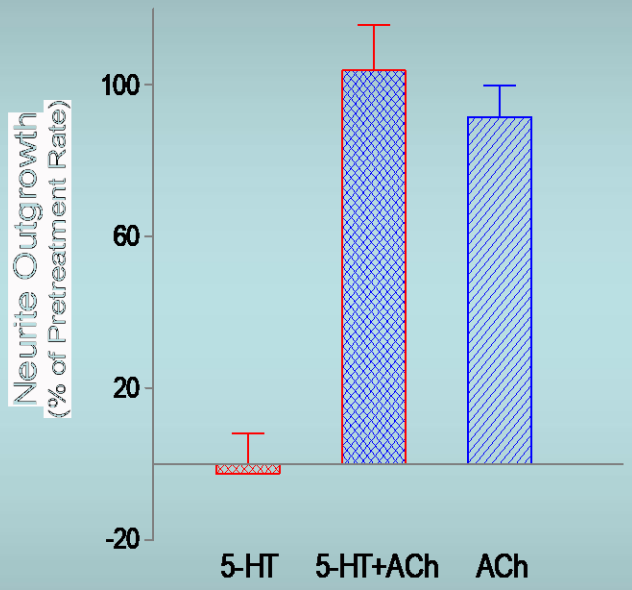




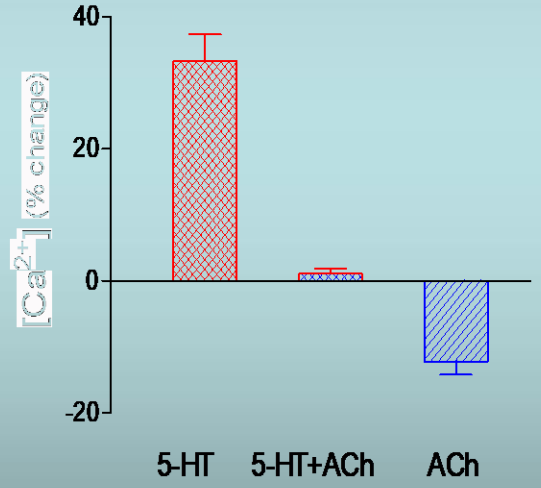
	Fiber length (μm)	ACh release (pmol/ganglion)	
		Basal	Stimulated
E12 3d	546.3±16.2	2.4±0.3	6.3±1.3
E12 7d	1633.3±43.2	13.8±2.8	38.4±4.0
E18 3d	690.0±40.0	4.1±0.6	10.7±1.0
E18 7d	749.3±40.1	7.8±1.4	15.5±2.3

Tata et al, 2003
Bernardini et al, 2004

EFFECT OF SEROTONIN (5-HT) AND ACETILCHOLINE (ACh)
ON ELONGATION OF HELISOMA NEURON B19 NEURITES

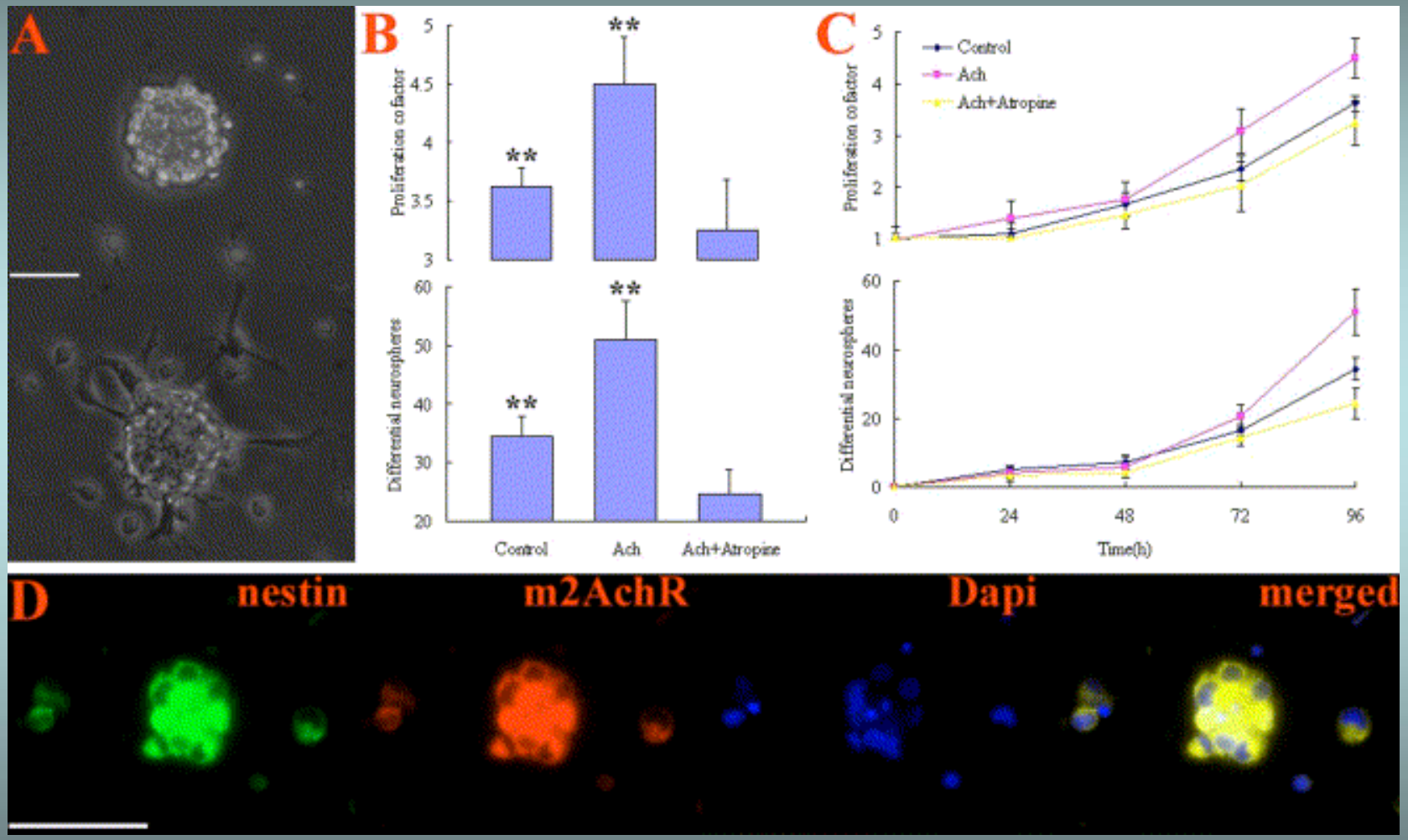


EFFECT OF 5-HT AND ACh ON CALCIUM LEVELS



McCobb et al., Neuron 1: 377-385; 1988

Neural precursors express cholinergic receptors



Zhou et al, 2004

NEUROGENESIS
2016, VOL. 3, NO. 1, e1127310 (13 pages)
http://dx.doi.org/10.1080/23262133.2015.1127310

Taylor & Francis
Taylor & Francis Group

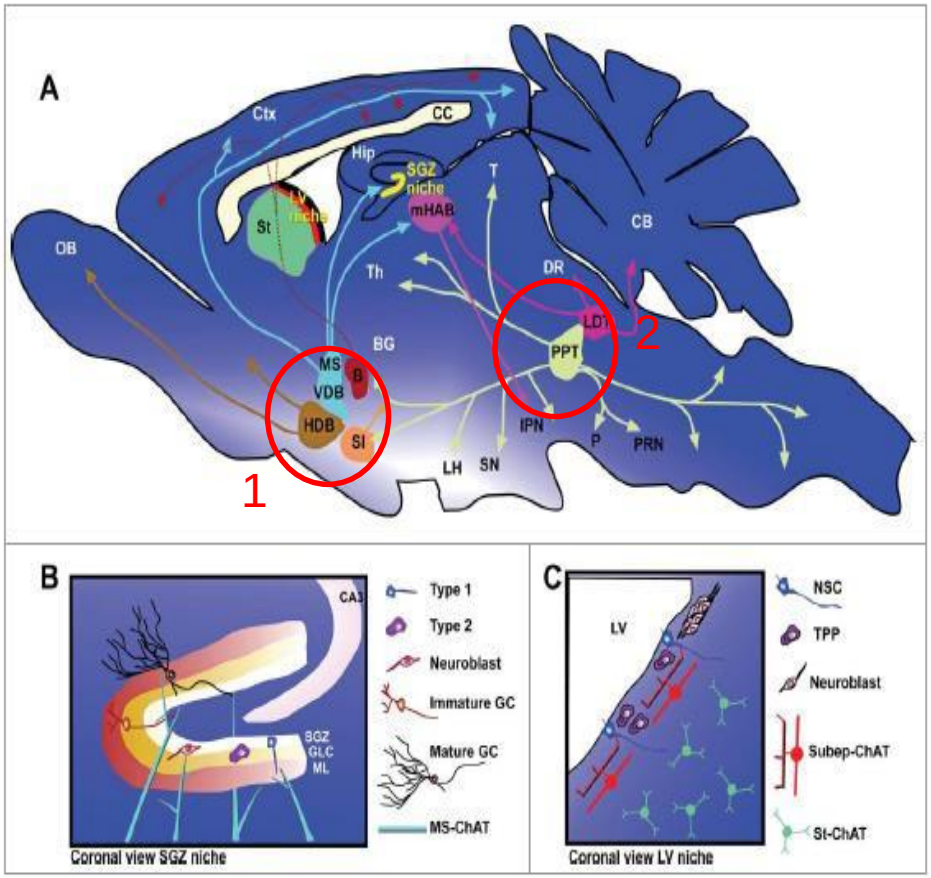
REVIEW

OPEN ACCESS

Cholinergic circuit control of postnatal neurogenesis

Brent Asrican[a], Patricia Paez-Gonzalez[a], Joshua Erb[a,b], and Chay T. Kuo[a,b,c,d,e,f]

[a]Department of Cell Biology, Duke University School of Medicine, Durham, NC, USA; [b]Neurobiology Graduate Training Program, Duke University School of Medicine, Durham, NC, USA; [c]Brumley Neonatal Perinatal Research Institute, Duke University School of Medicine, Durham, NC, USA; [d]Department of Neurobiology, Duke University School of Medicine, Durham, NC, USA; [e]Preston Robert Tisch Brain Tumor Center, Duke University School of Medicine, Durham, NC, USA; [f]Duke Institute for Brain Sciences, Duke University School of Medicine, Durham, NC, USA



1. Nucleus Basalis Group;
2. Pontine Cholinergic Group

Cholinergic interneurons are also present in caudate putamen, striatum, nucleus accumbens, olfactory bulb, hippocampus, cerebral cortex, hypotalamus, spinal cord

Cholinergic projections can reach different neurogenic niches

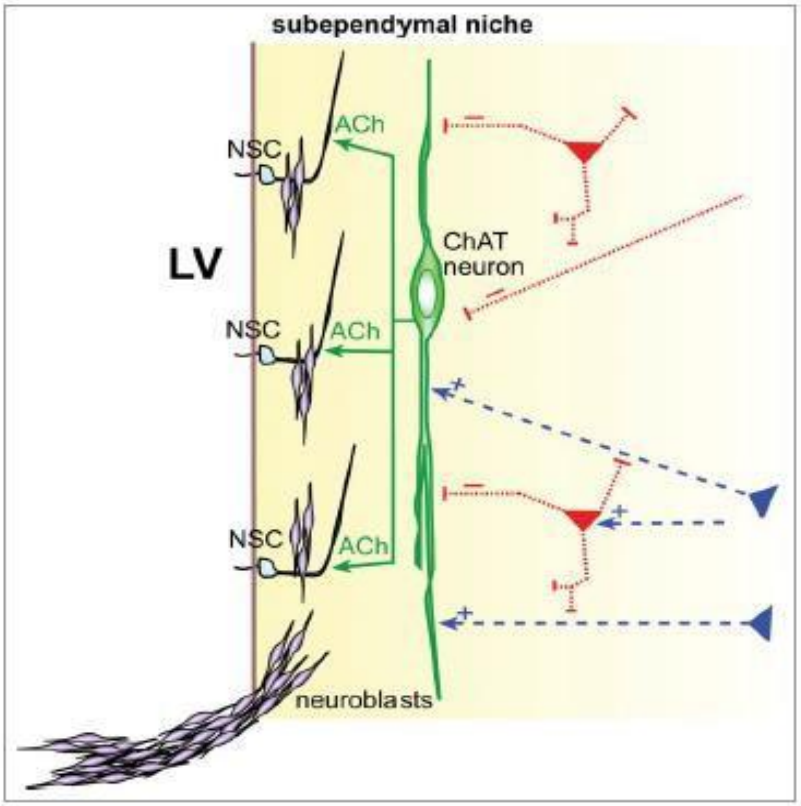


Figure 3. Subependymal cholinergic neuron bridging SEZ niche/neurogenesis to neural circuit-level control. Schematic representation of subep-ChAT neuron (green) providing ACh to modulate adult SEZ neural stem cells (NSC) production of new neuroblasts, which then migrate and assemble into neuroblast chains. Dashed lines represent putative excitatory (+, blue) or inhibitory (−, red) inputs onto subep-ChAT neuron dendrites. LV = lateral ventricle.

Cholinergic neurons have been identified in the LV niche

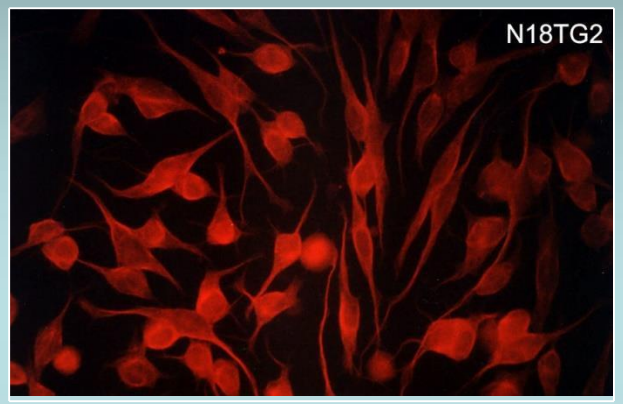
The alteration of excitability of these neurons causes a significant reduction of DCX+ neuroblasts in LV

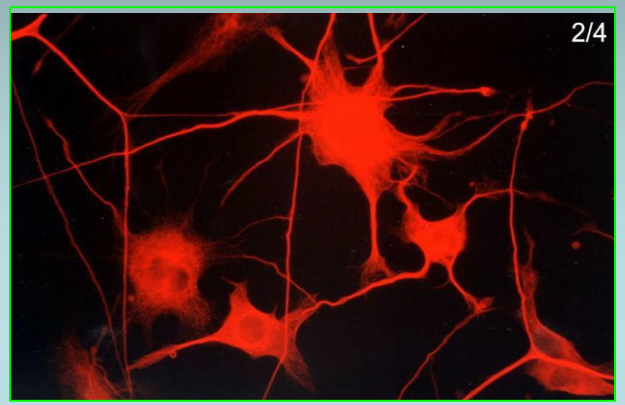
Cholinergic circuit activity is required to substain adult LV neurogenesis

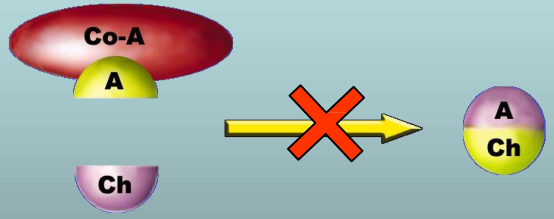
Asrican et al, 2016

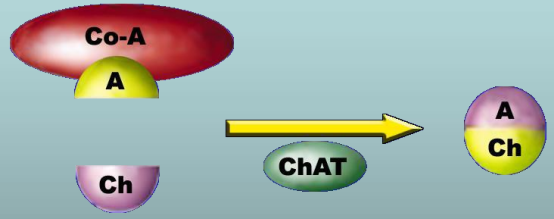
ChAT-positive clones

Transfection of mouse neuroblastoma cells



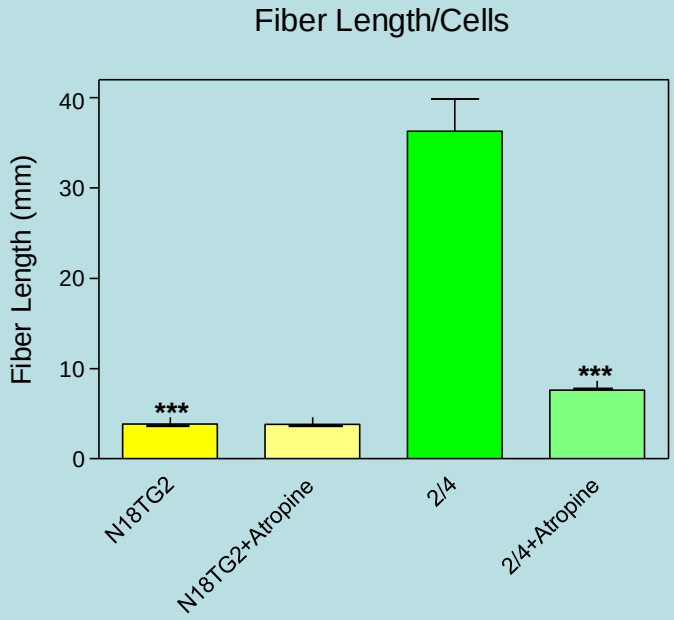






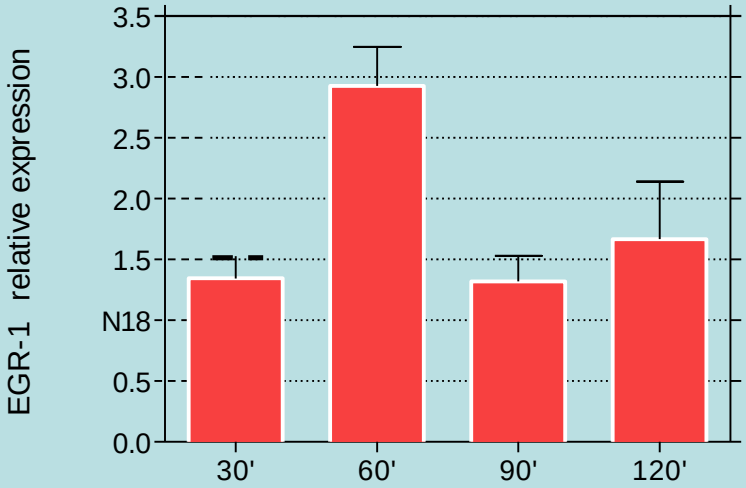
Neuroblasti immaturi
Non differenziano correttamente
Non producono ACh

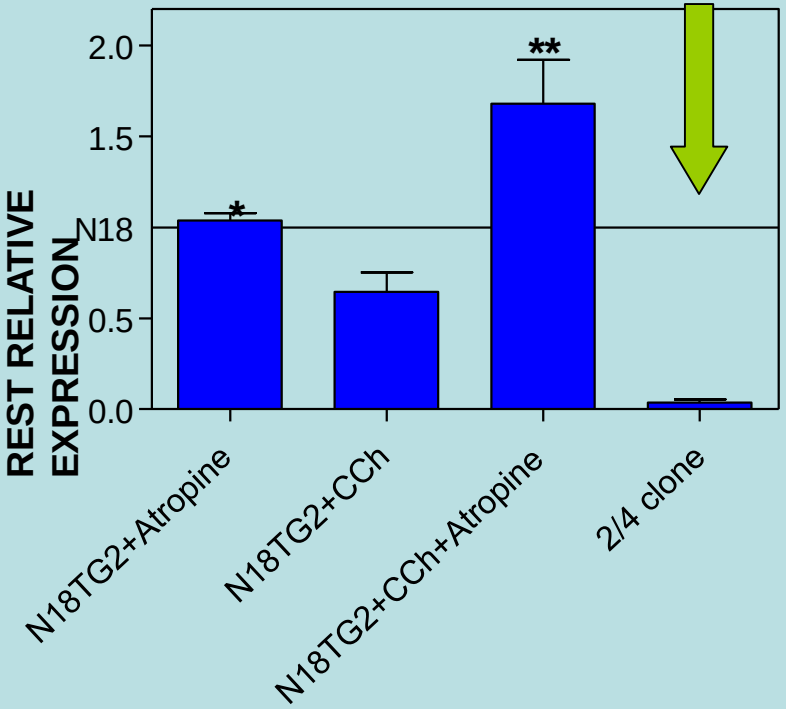
Bignami et al., 1997 J. Neurochem



1. Esprimono canali Na+ voltaggio dipendenti
2. Sinapsina 1

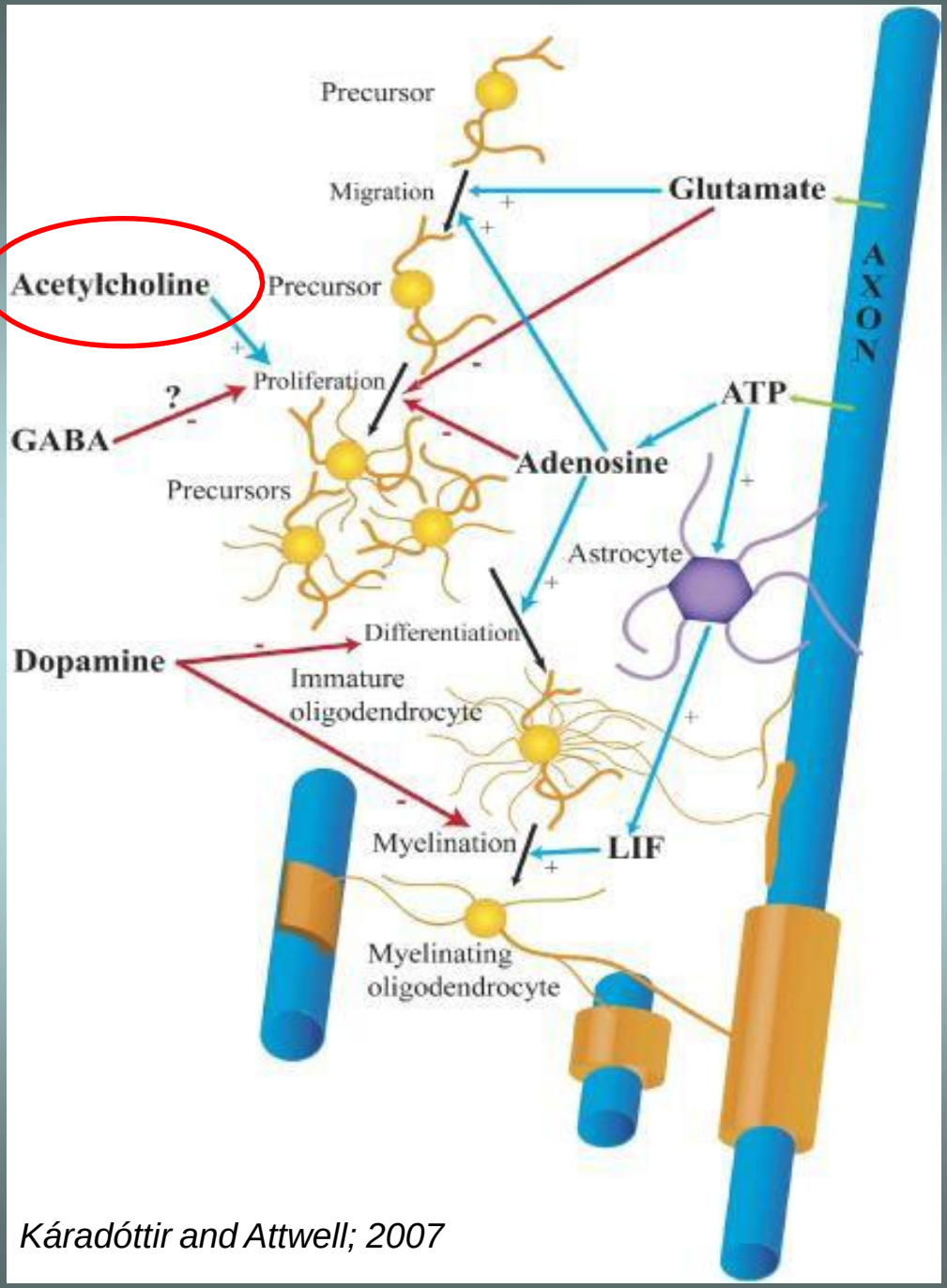
A





Salani et al, J Neurochem. 2009

Glial cells express neurotransmitter receptors



Káradóttir and Attwell; 2007

Recettori per neurotrasmettitori sono stati individuati:

1. Negli oligodendrociti
2. Nella microglia
3. Negli astrociti

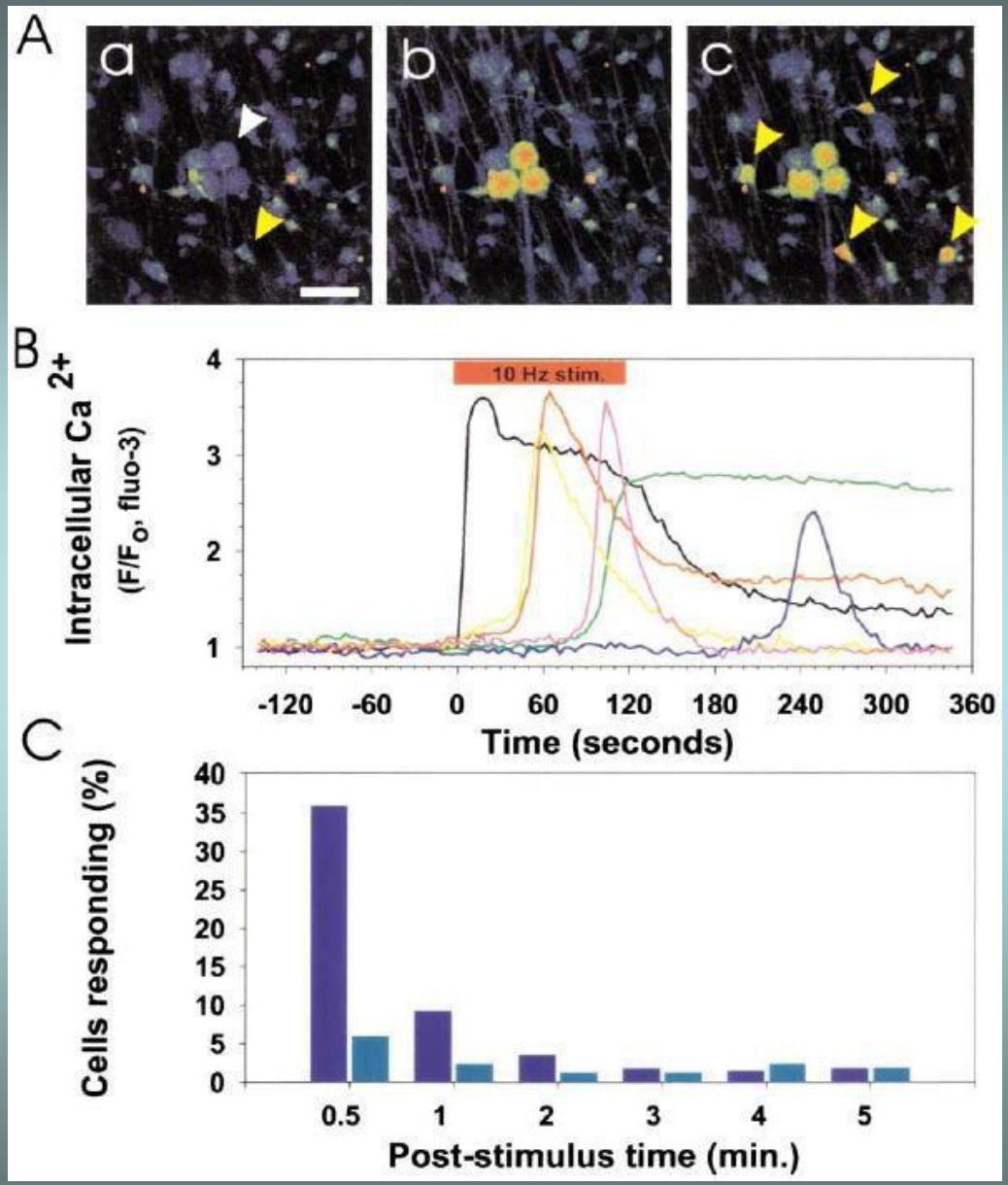
In tutte le popolazioni gliali i neurotrasmettitori possono:

1. Modulare la proliferazione
2. Regolare la fase differenziativa
3. Modulare la funzione della glia

Le cellule gliali posseggono canali ionici voltaggio sensibili e recettori per neurotrasmettitori, ma non generano potenziali di azione.

Metodi di studio:

1. ***Imaging*** **di calcio**
2. **Co-Colture cellulari**



Adenosina
e rec. Purinergici

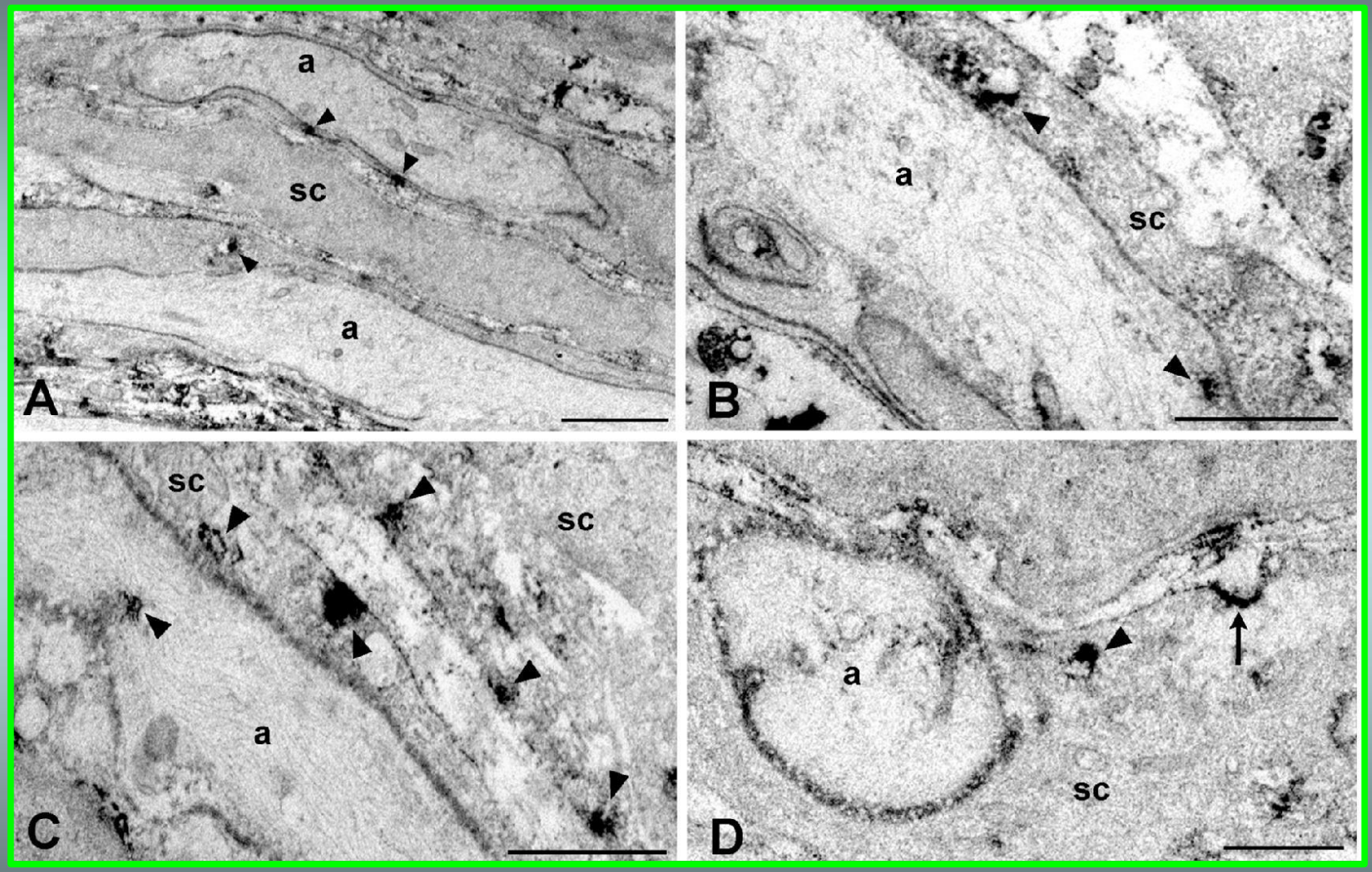
Fields and Steven, 2000

Espressione di recettori muscarinici nelle cellule di Schwann

E12

P5

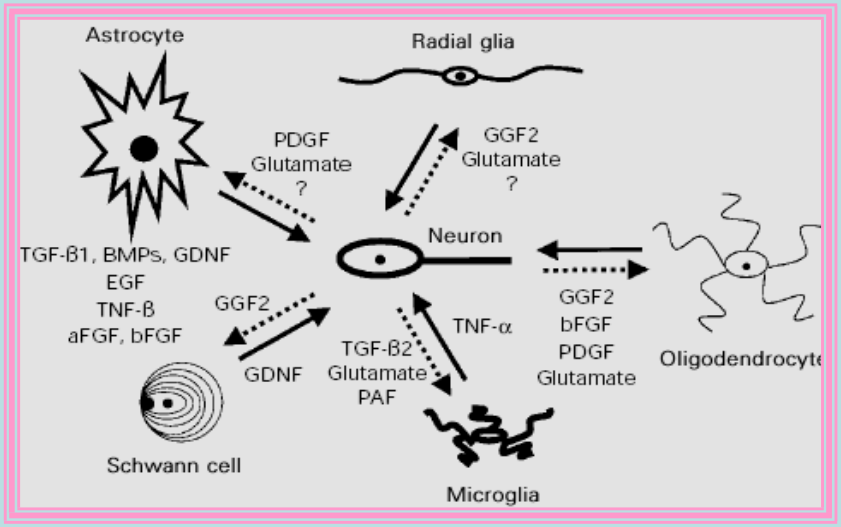
Bernardini et al, 1998



Loreti et al, 2007

Le cellule gliali sia del SNC che del SNP esprimono recettori per l'ACh

Cellule di Schwann → **Attivazione recettore M2**



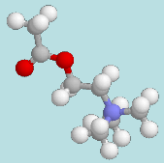
Inibizione della proliferazione cellulare
Avanzamento nel programma differenziativo

Loreti et al,J Neurosci Res 84, 2006
Loreti et al, Neuron Glia Biology 3, 2007
Uggenti et al, Dev Neurobiol 2014
Piovesana et al, 2020
Piovesana et al 2022

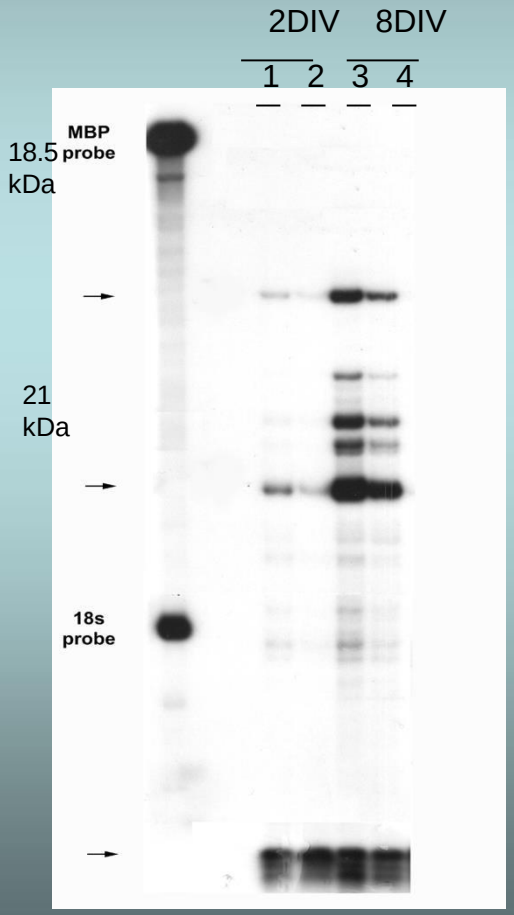
Oligodendrociti → **Attivazione recettore M3**

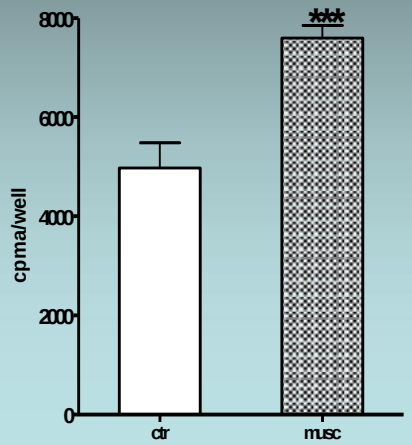
Ragheb et al, 2001
Cui et al, 2006
De Angelis et al, 2012

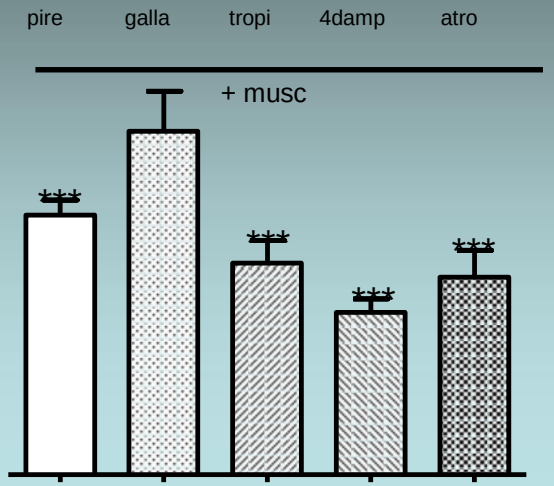
Incremento Proliferazione
Blocco del differenziamento

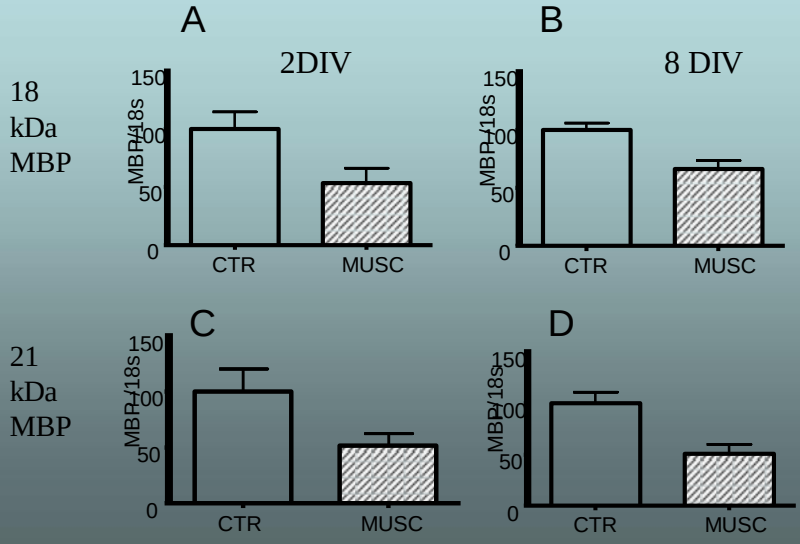


ACh stimola la proliferazione ma inibisce il differenziamento in OPC



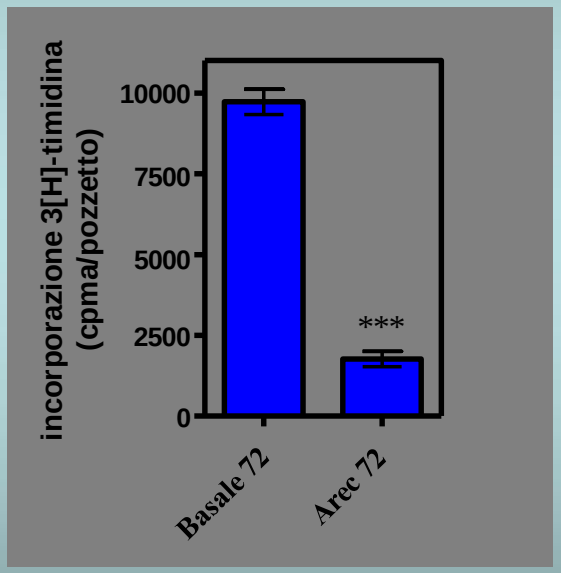






De Angelis et al, 2012

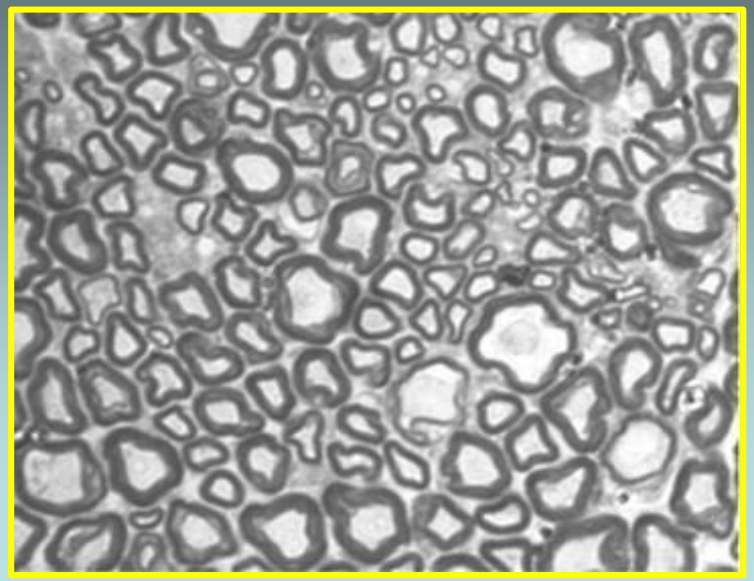
L'attivazione del recettore M2 inibisce la proliferazione delle cellule di Schwann



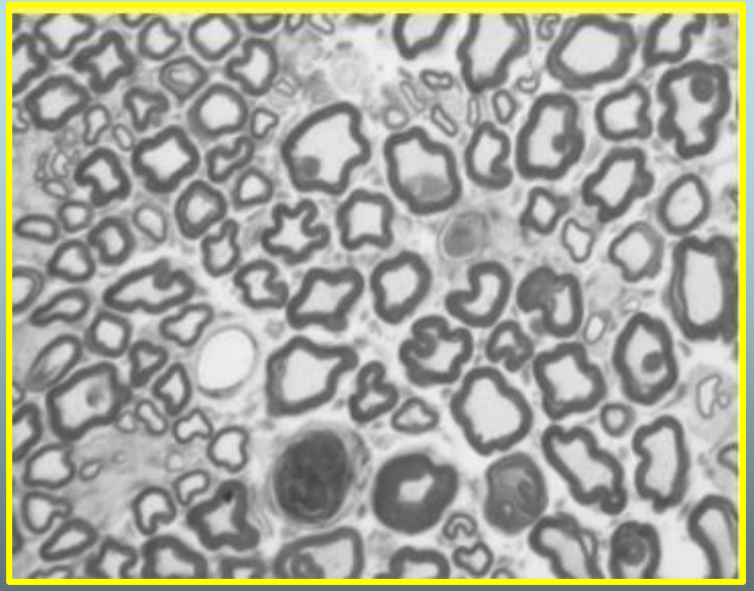
Trattamento	% G1	% S	% G2
Controllo	72,22	23,18	4,6
Arecaidina 16 hr	91,99	4,56	3,45
Arecaidina 24 hr	93,98	0,14	5,88
Arecaidina 48 hr	95,62	0,44	3,94
Arecaidina 72 hr	97,44	0,54	2,02

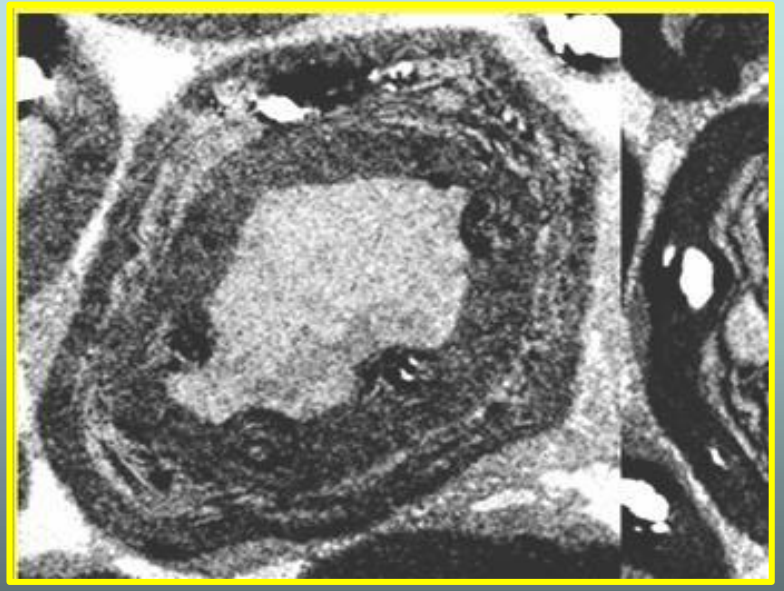
Loreti et al, Neuron Glia Biology 2007

WT

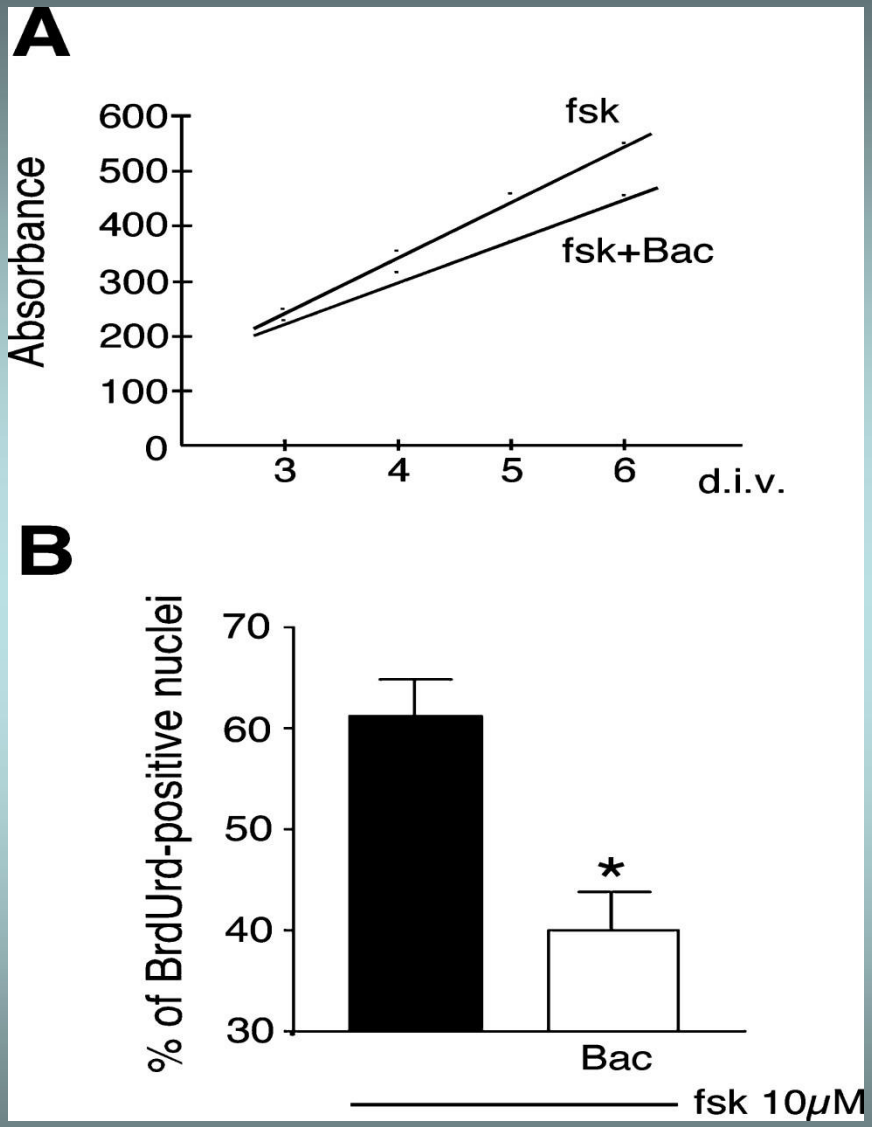


M2 -/-



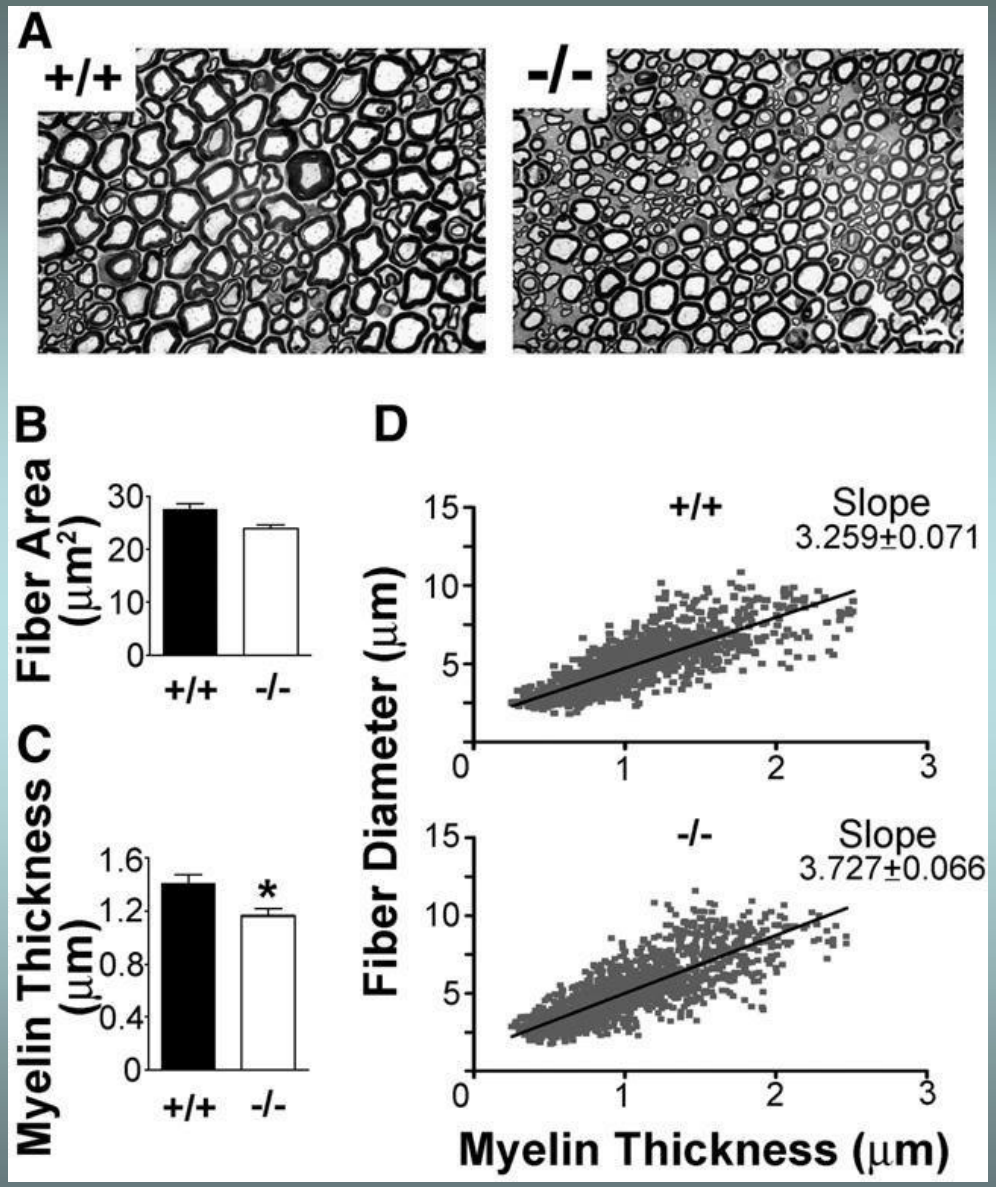


Effetto del GABA sulle cellule di Schwann



Magnaghi et al, 2004

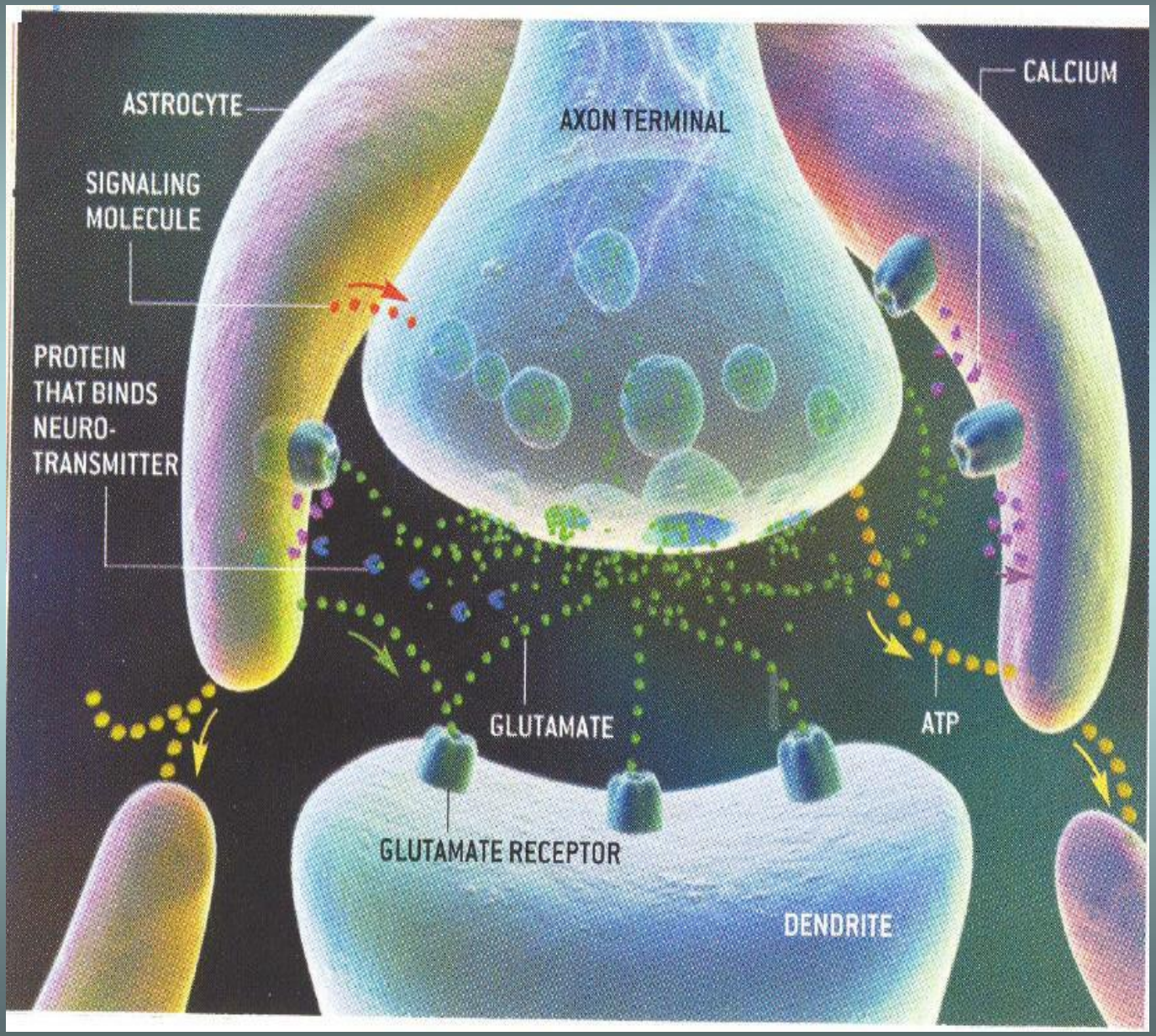
GabaBR -/-

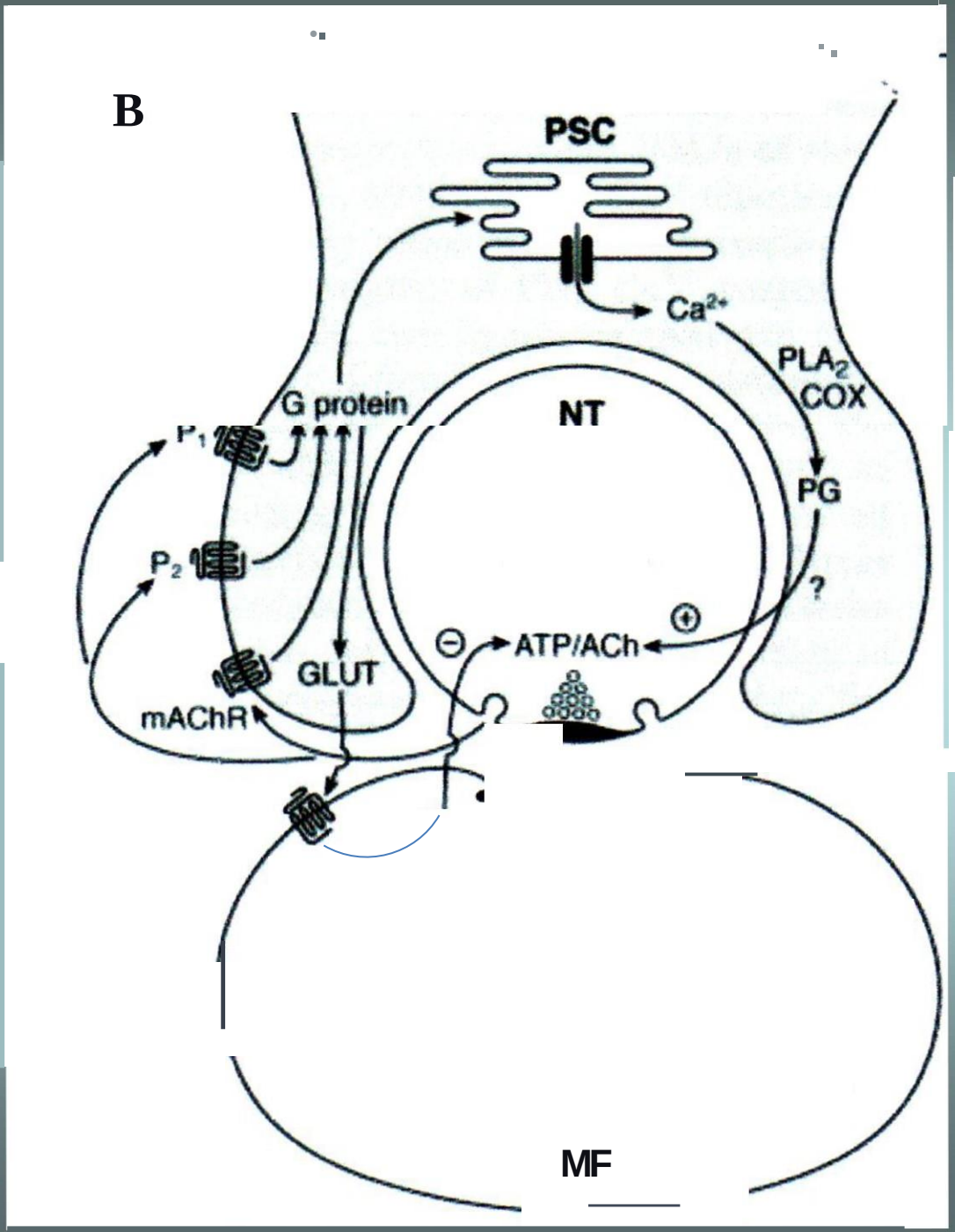


Magnaghi et al, 2008

- L’azione dei neurotrasmettitori GABA e ACh controlla la proliferazione e la mielinizzazione nelle cellule di Schwann

SINAPSI TRIPARTITA




B
PSC
Ca2+
PLA2
COX
G protein
NT
P1
P2
PG
?
ATP/ACh
GLUT
mAChR
MF

- I neurotrasmettitori modulano l’interazione glia e neurone alla sinapsi
- Questa interazione ha un effetto sulla modulazione della attività della sinapsi

Concludendo……..

- I neurotrasmettitori controllano proliferazione, sopravvivenza e crescita neuritica nelle cellule neuronali e modulano l'attività sinaptica

I Neurotrasmettitori mediano l'interazione neurone-glia . Intervengono nella regolazione della proliferazione, differenziamento della cellula gliale e collaborano ai processi di mielinizzazione