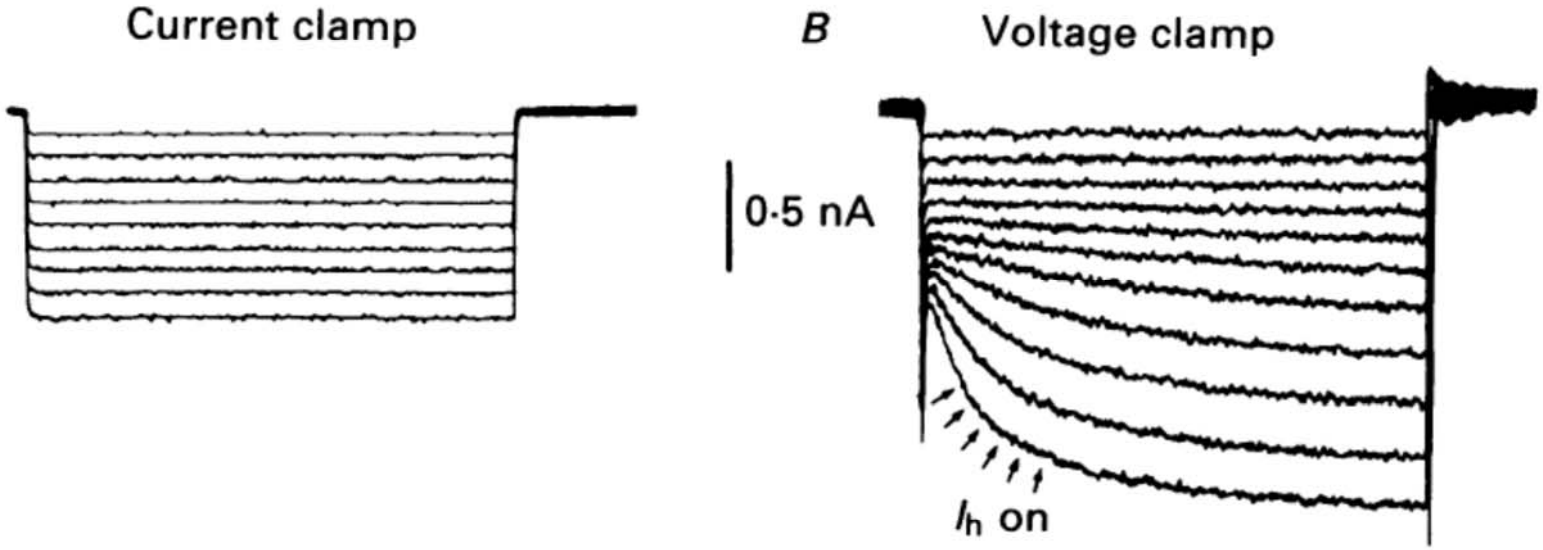
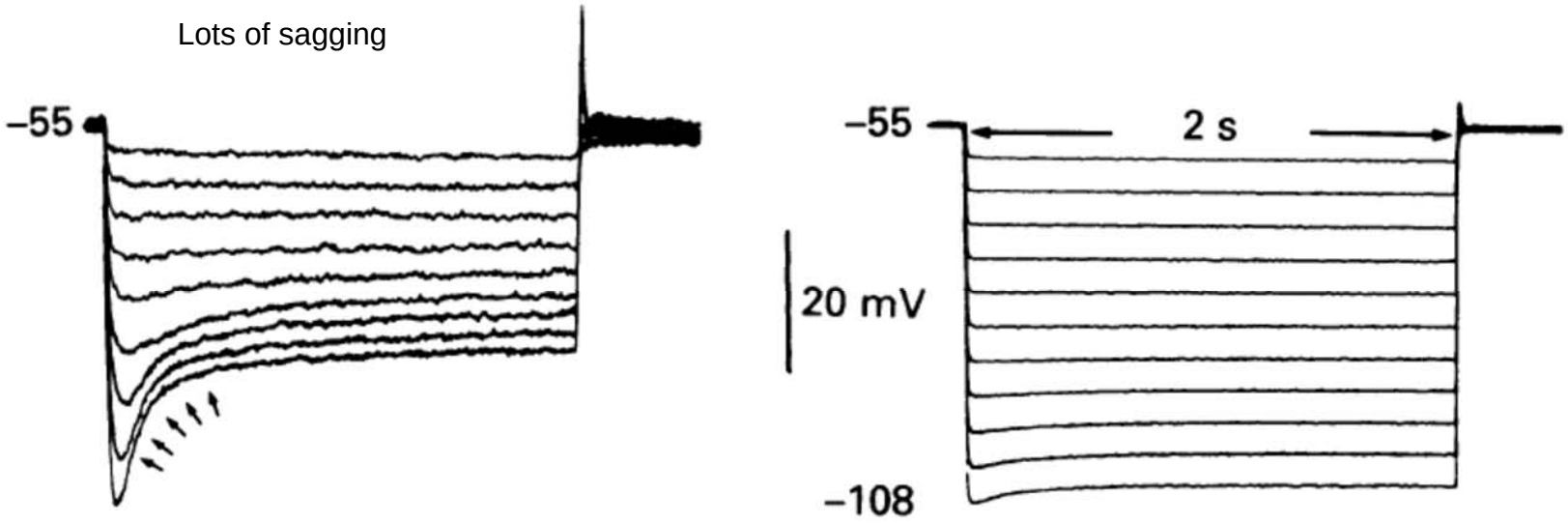
Journal of Physiology (1990), **431**, *pp.* 291–318

I_h IN THALAMIC NEURONES

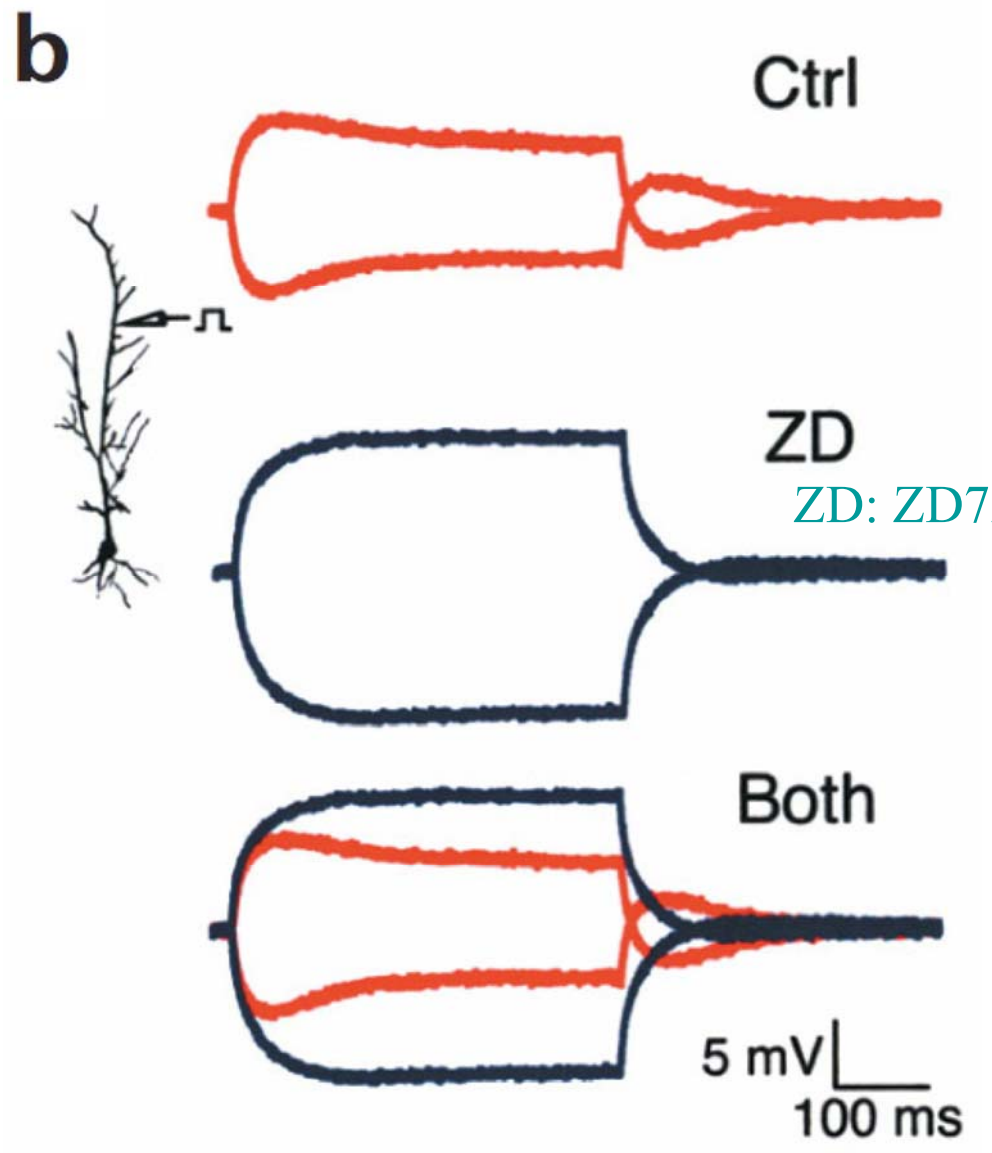


H current is very slow

Lots of sagging

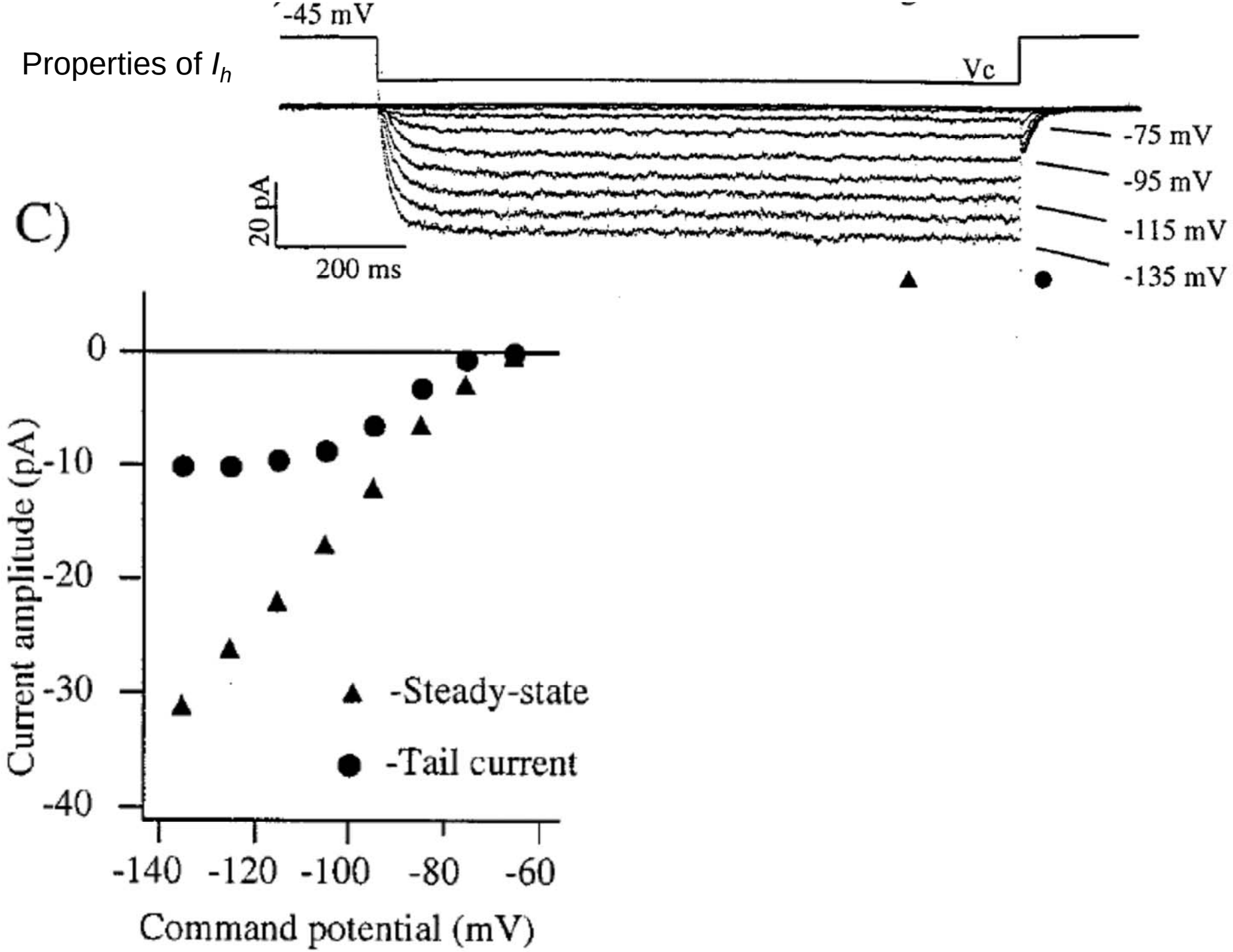


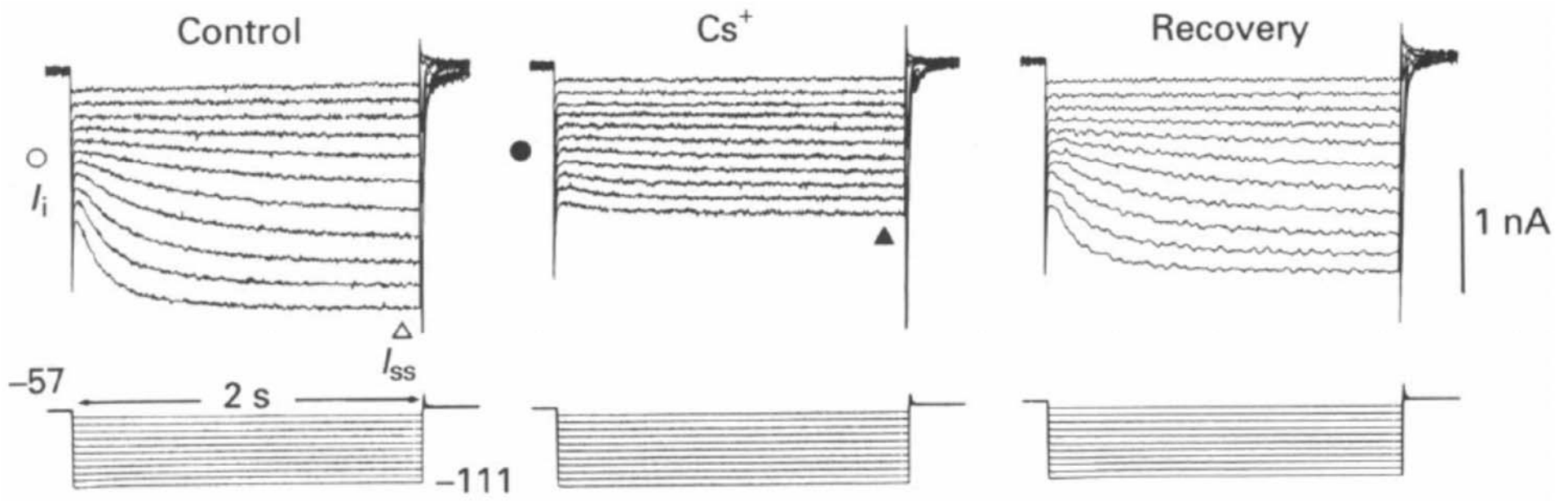
When I_h is active at resting V_m.



ZD: ZD7288 I_h blocker

Properties of I_h



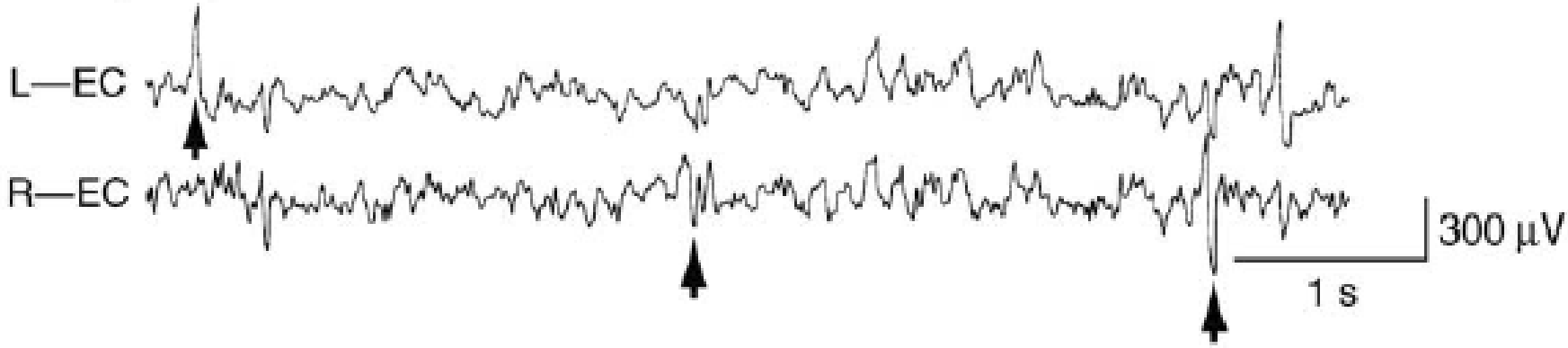

Control
Cs+
Recovery
○
I_i
△
I_{ss}
●
▲
1 nA
–57
2 s
–111

EC: entorhinal cortex

A In vivo EEG recordings

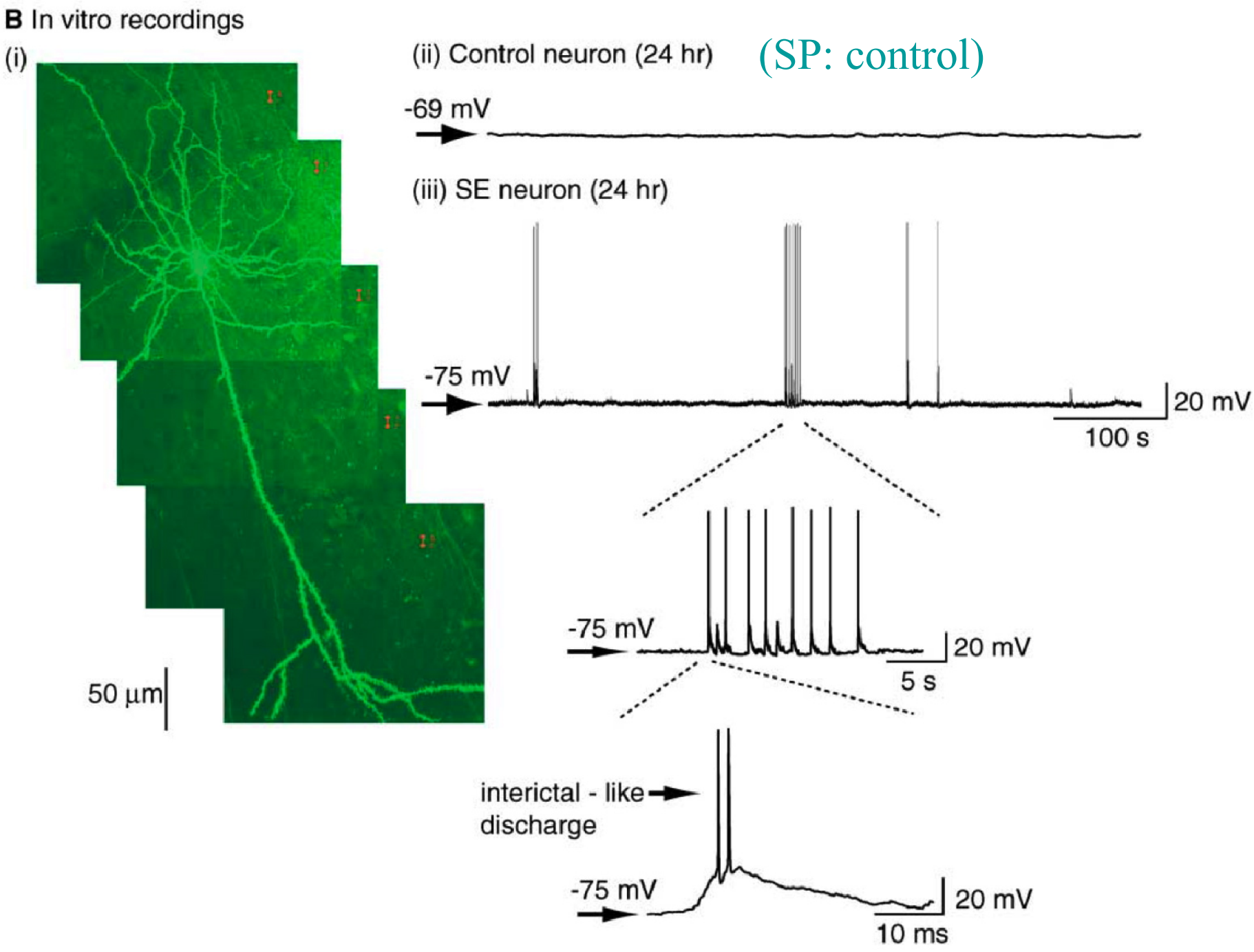
i) Control neurons (24 hr)

ii) SE neurons (24 hr)

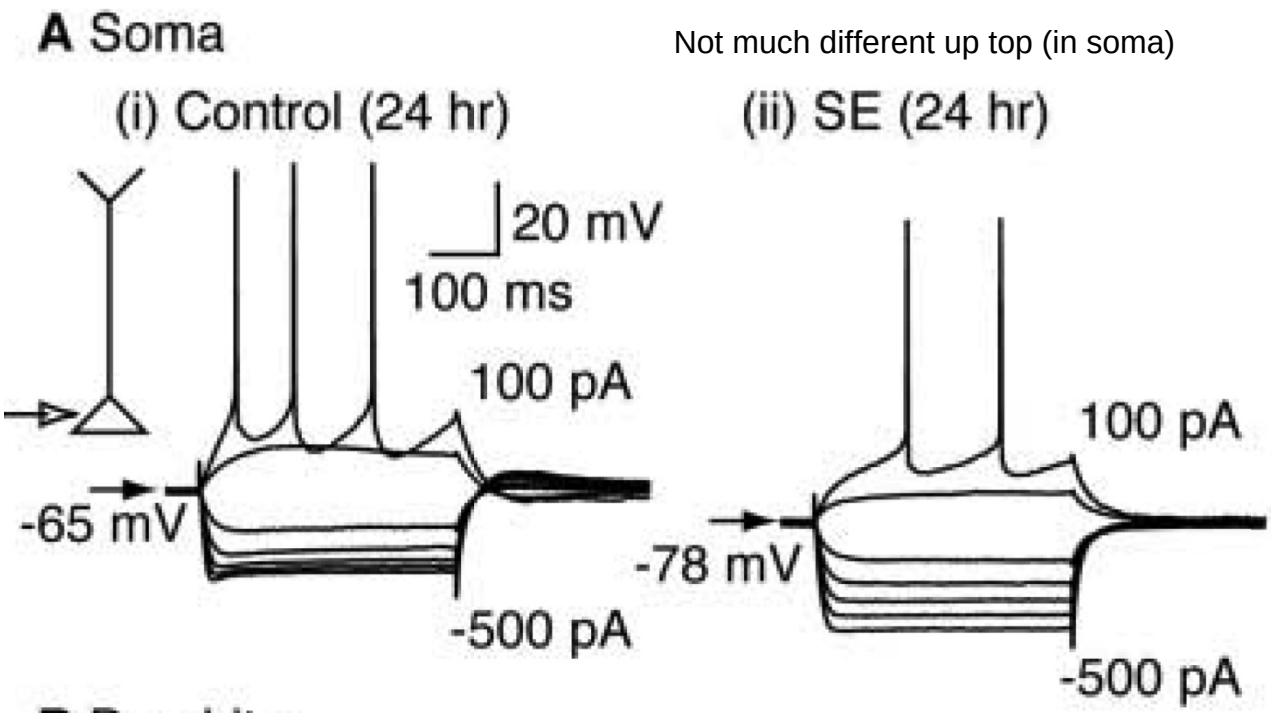


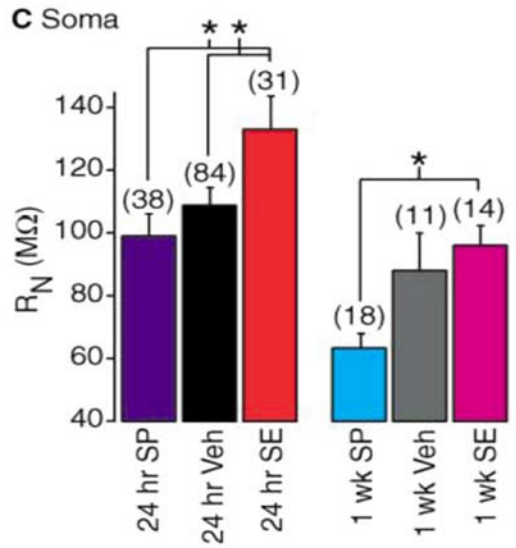
SE: electrographic status epilepticus
Kainate (i.p.) 1-2 hr later followed by sodium pentobarbital (SP); chronic seizure develops 2-4 weeks later.

Neuron, Vol. 44, 495–508, October 28, 2004


B In vitro recordings
(i)
50 µm
(ii) Control neuron (24 hr)
(SP: control)
-69 mV
(iii) SE neuron (24 hr)
-75 mV
20 mV
100 s
-75 mV
20 mV
5 s
interictal - like
discharge
-75 mV
20 mV
10 ms

Not much different up top (in soma)

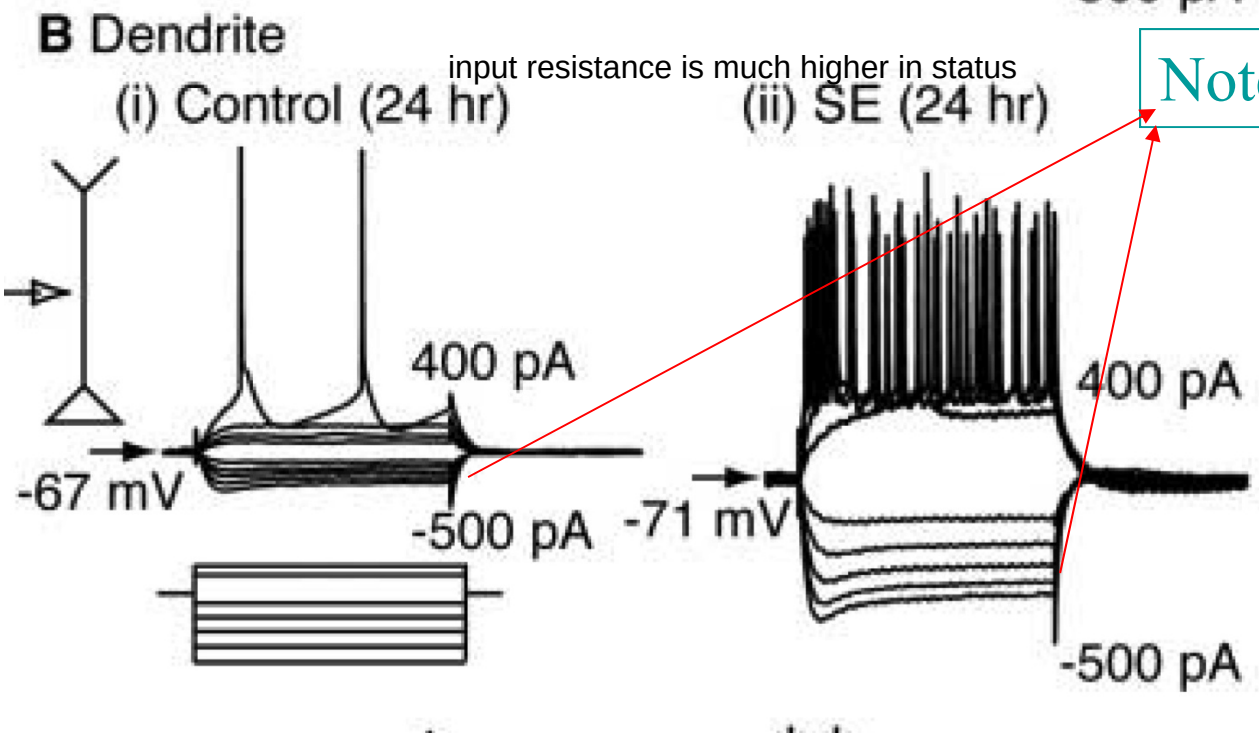


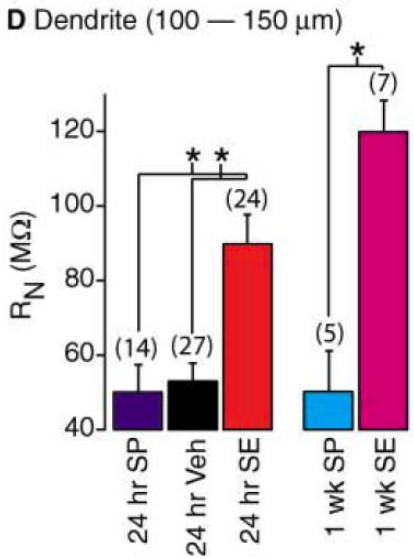


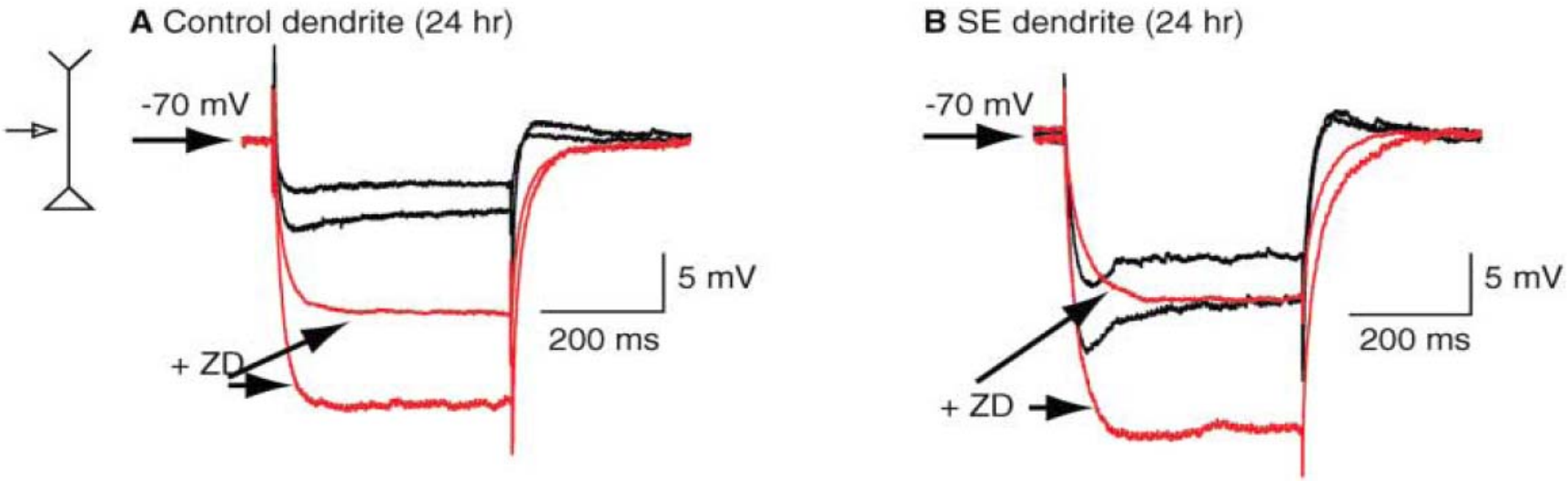
In this case Ih is the most dominant contributor to Rin

input resistance is much higher in status

Note the difference in R_{in}.

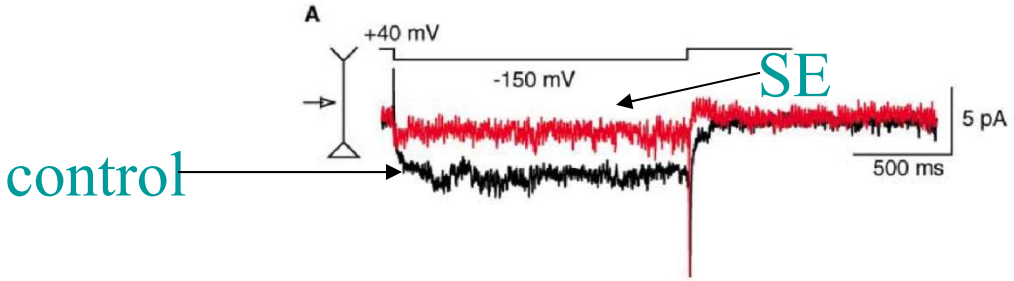


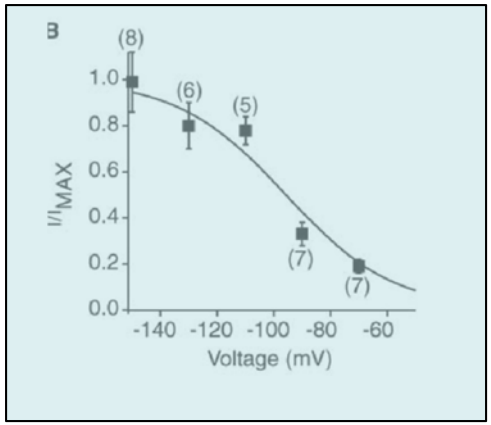


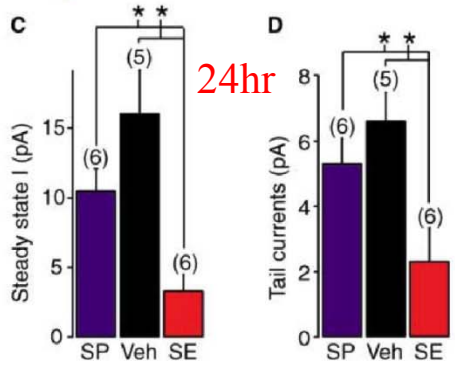


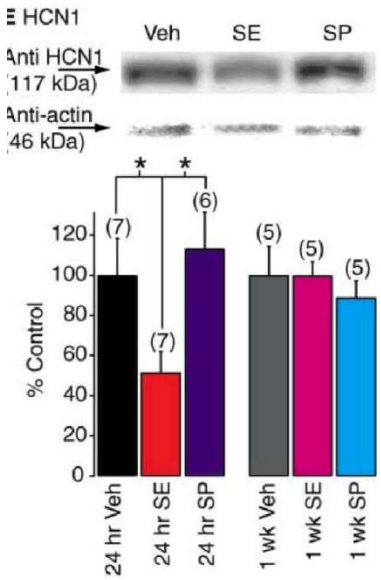
ZD: ZD7288 I_h blocker, note the difference in the fraction of potential blocked by ZD.

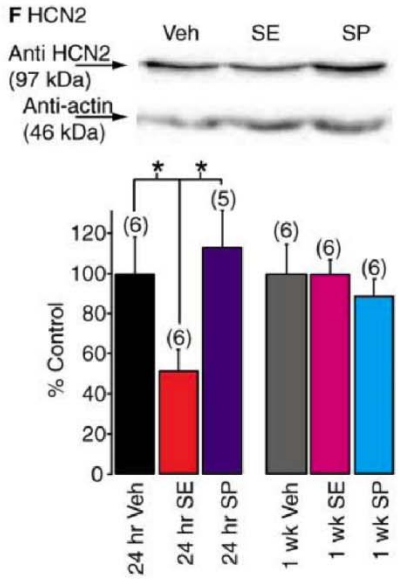
I_h=HCN (hyperpolarization cyclic nucleotide activated channels)







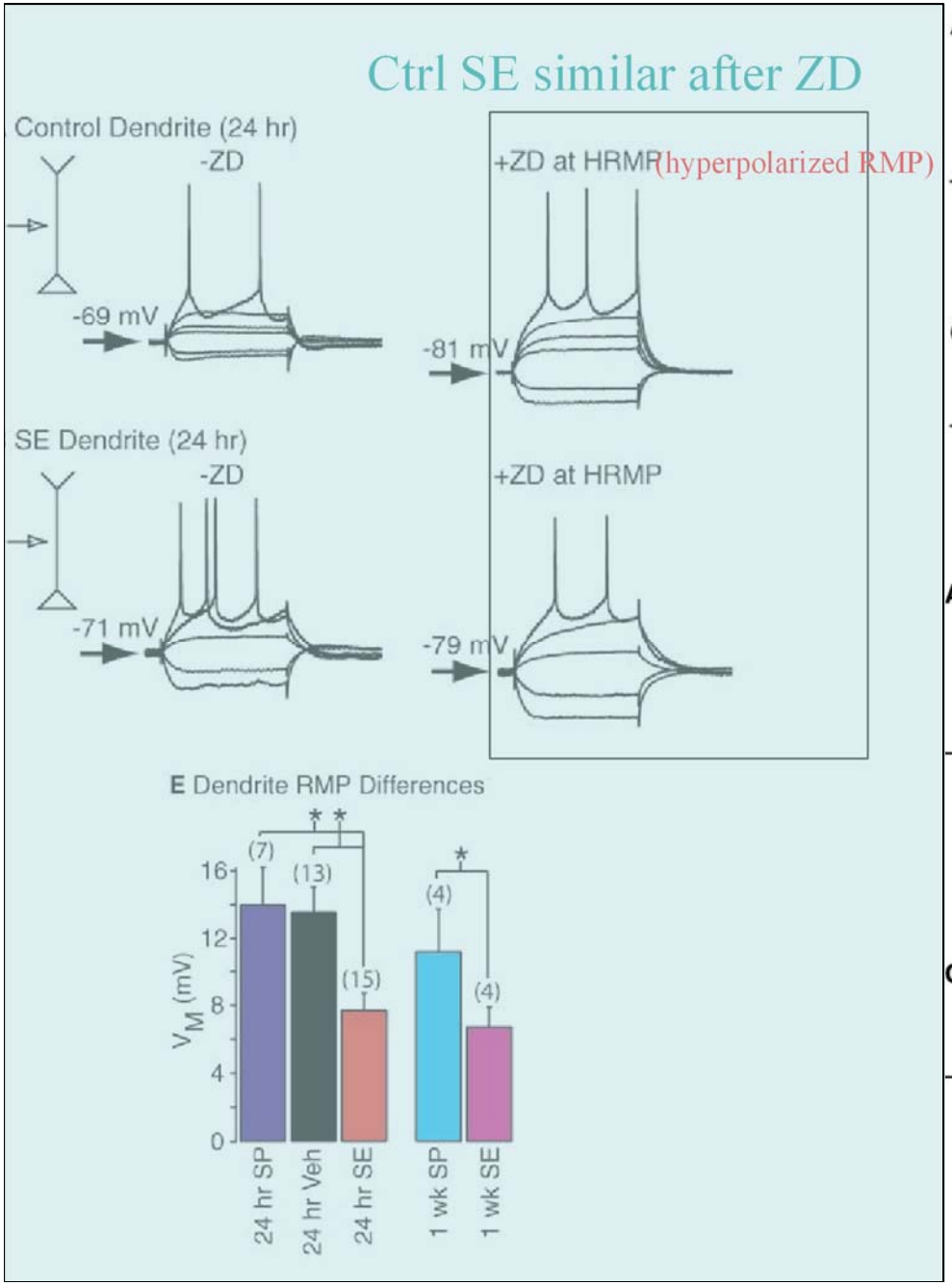


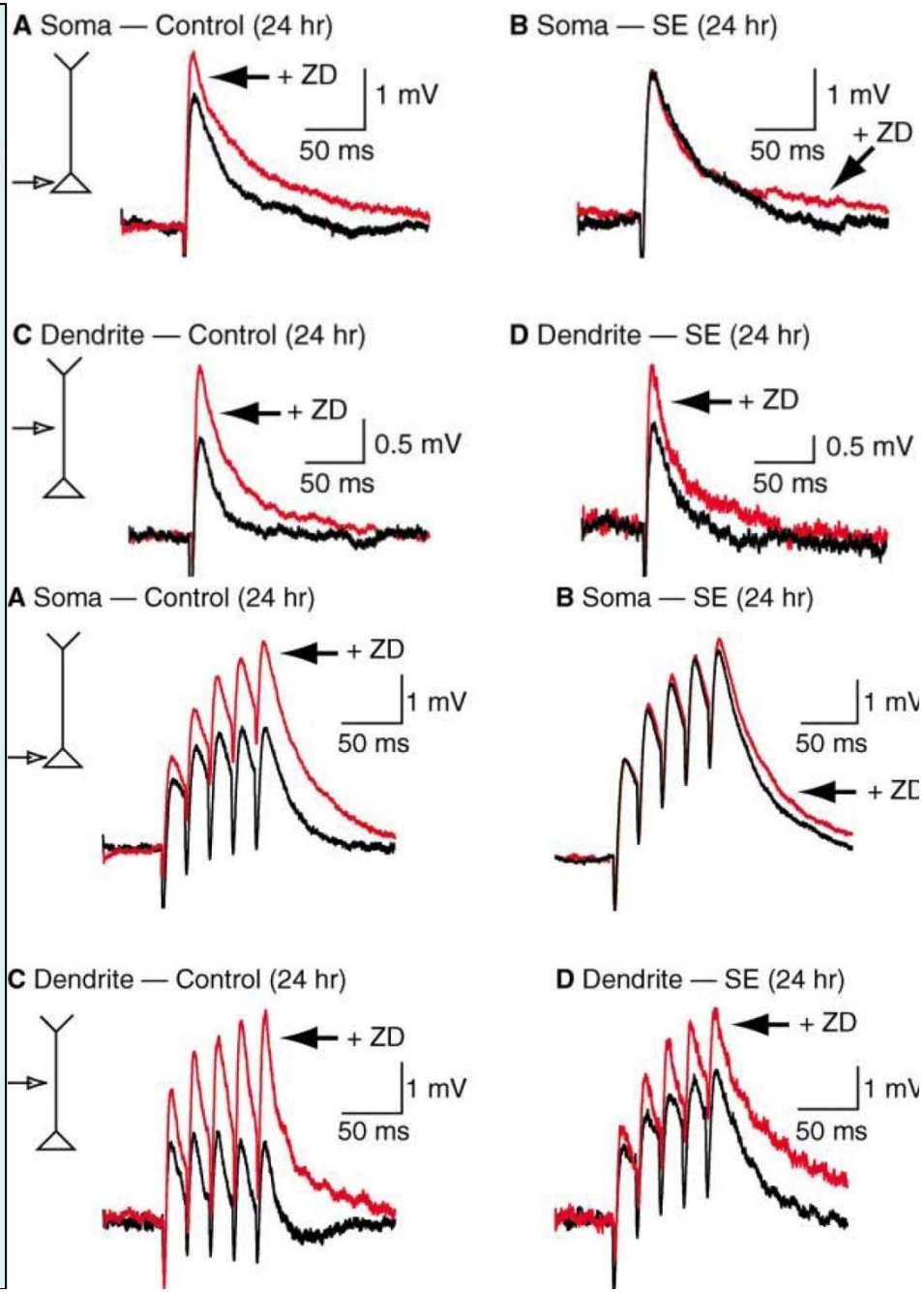


But I_h is still low in 1 wk SE

Ih has a much more efficient effect at blocking EPSP in dendriates than it does in axons

Functions of I_h in dendrites: I_h is open at resting V_m and ↓ R_{in}.➔has impact on EPSP.



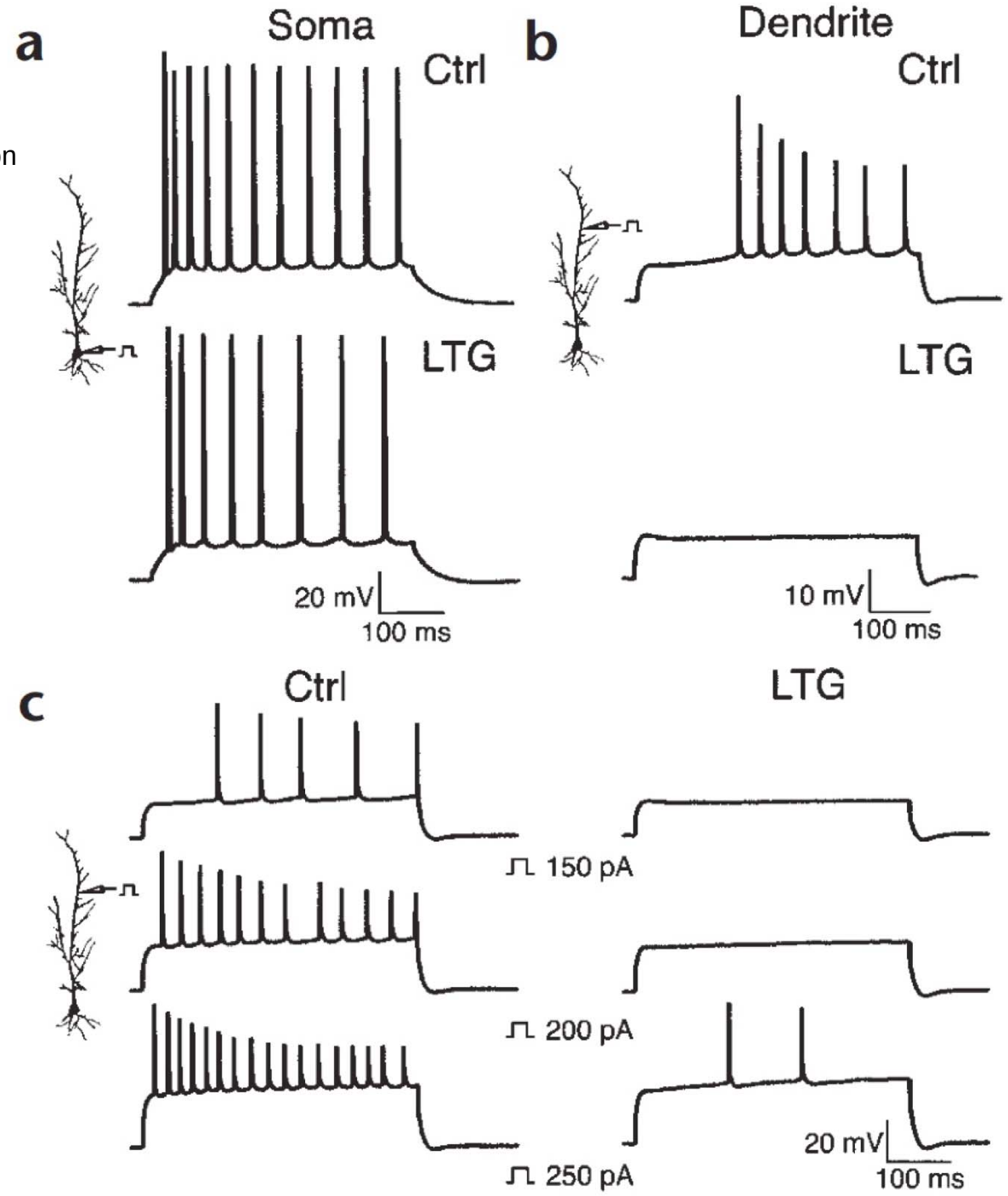


here, the response is similar in black line (lower) because of Ih

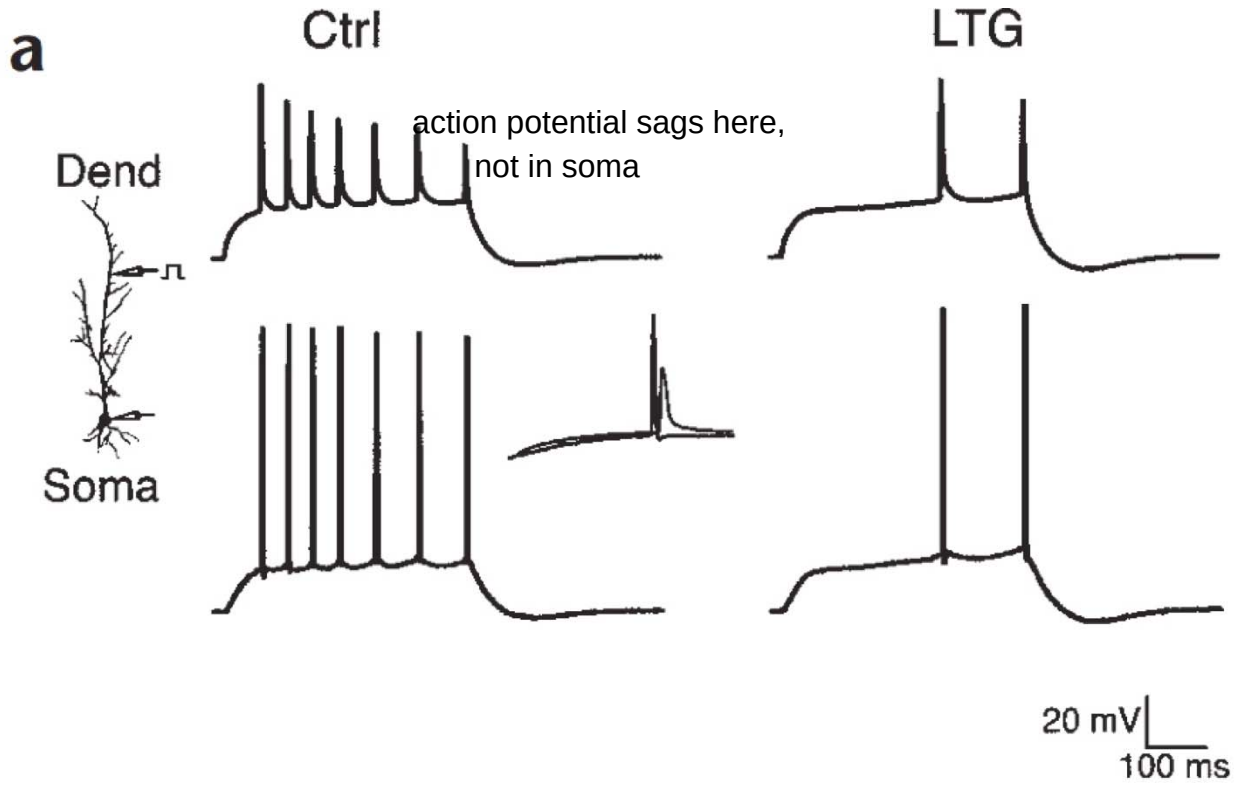
LTG: lamotrigine

sodium channel blocker; used to treat seizures, bipolar, depression

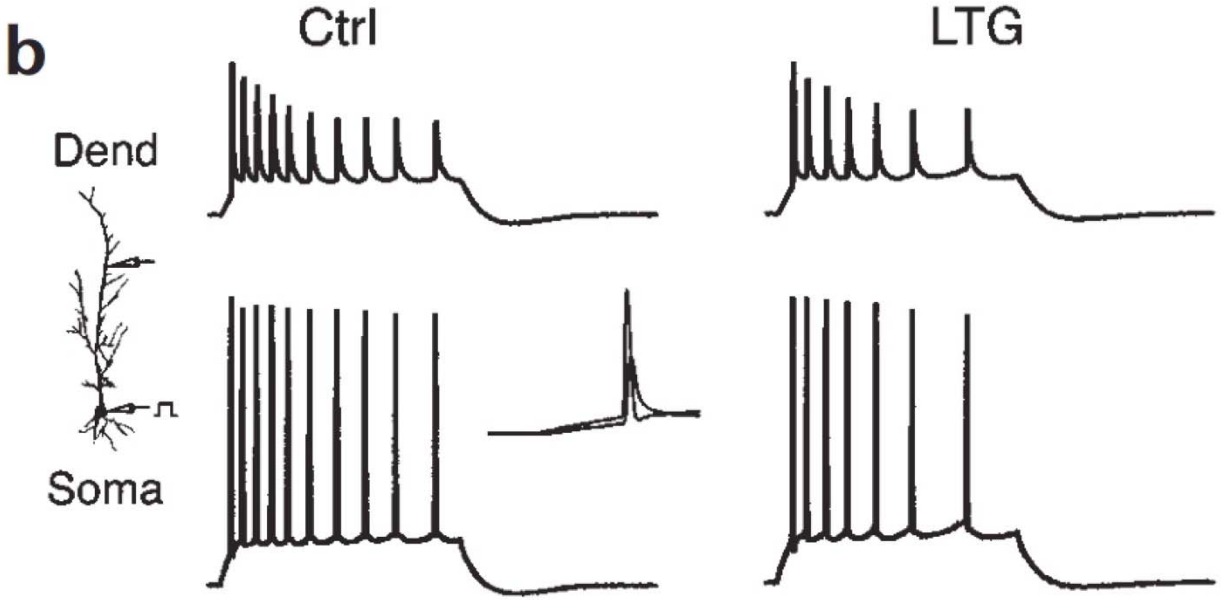
opens Ih channels!

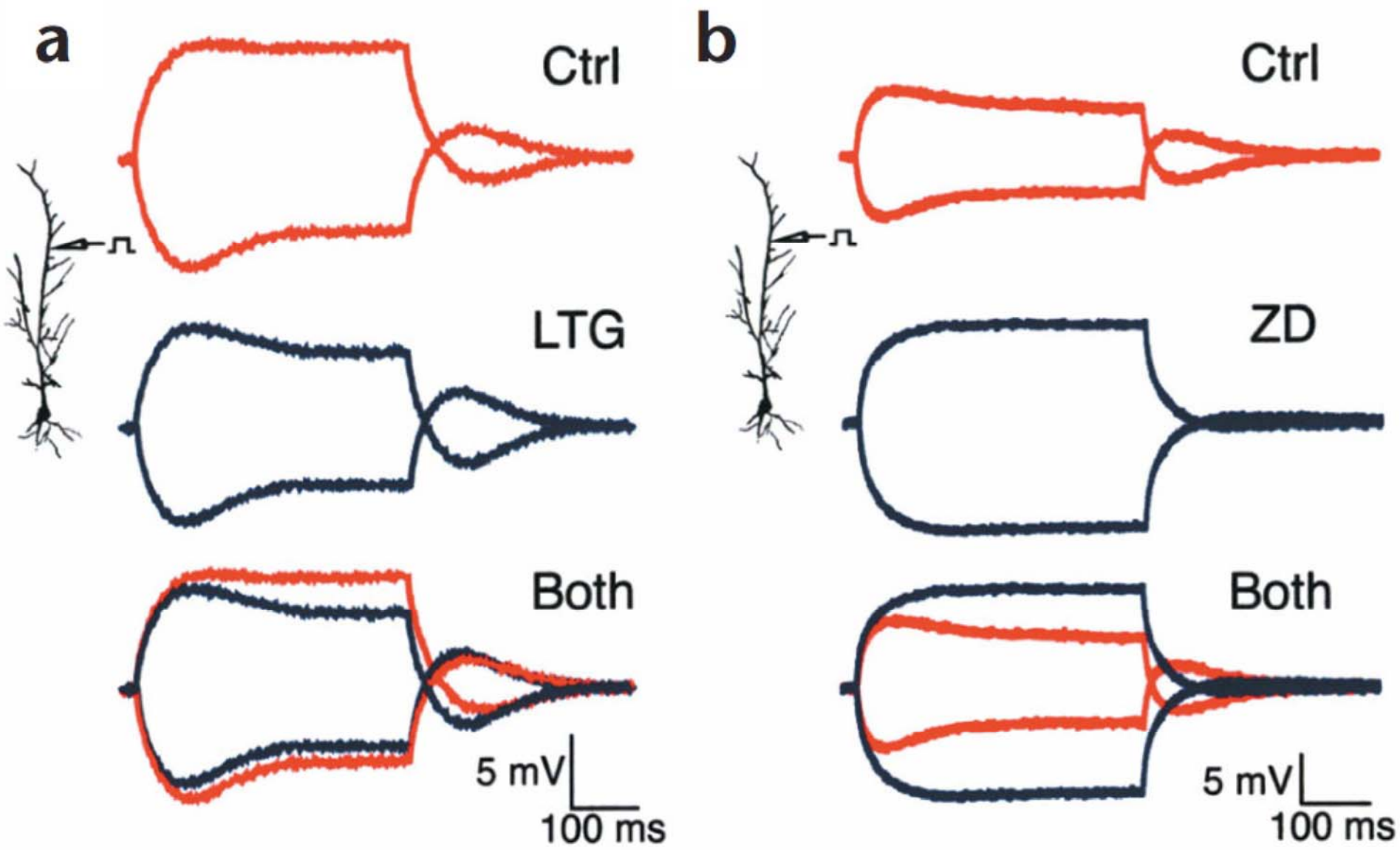


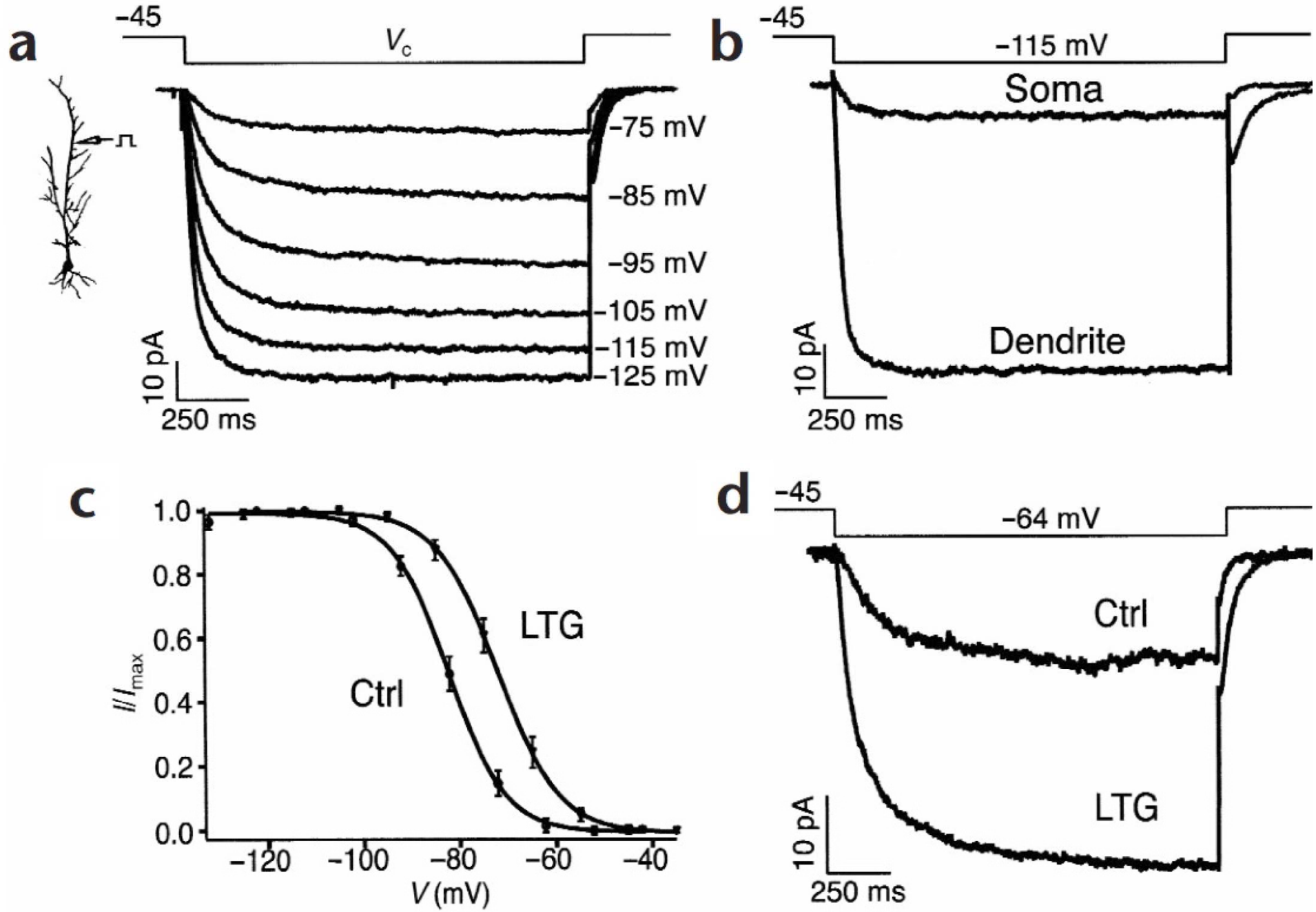
Dendritic I injection



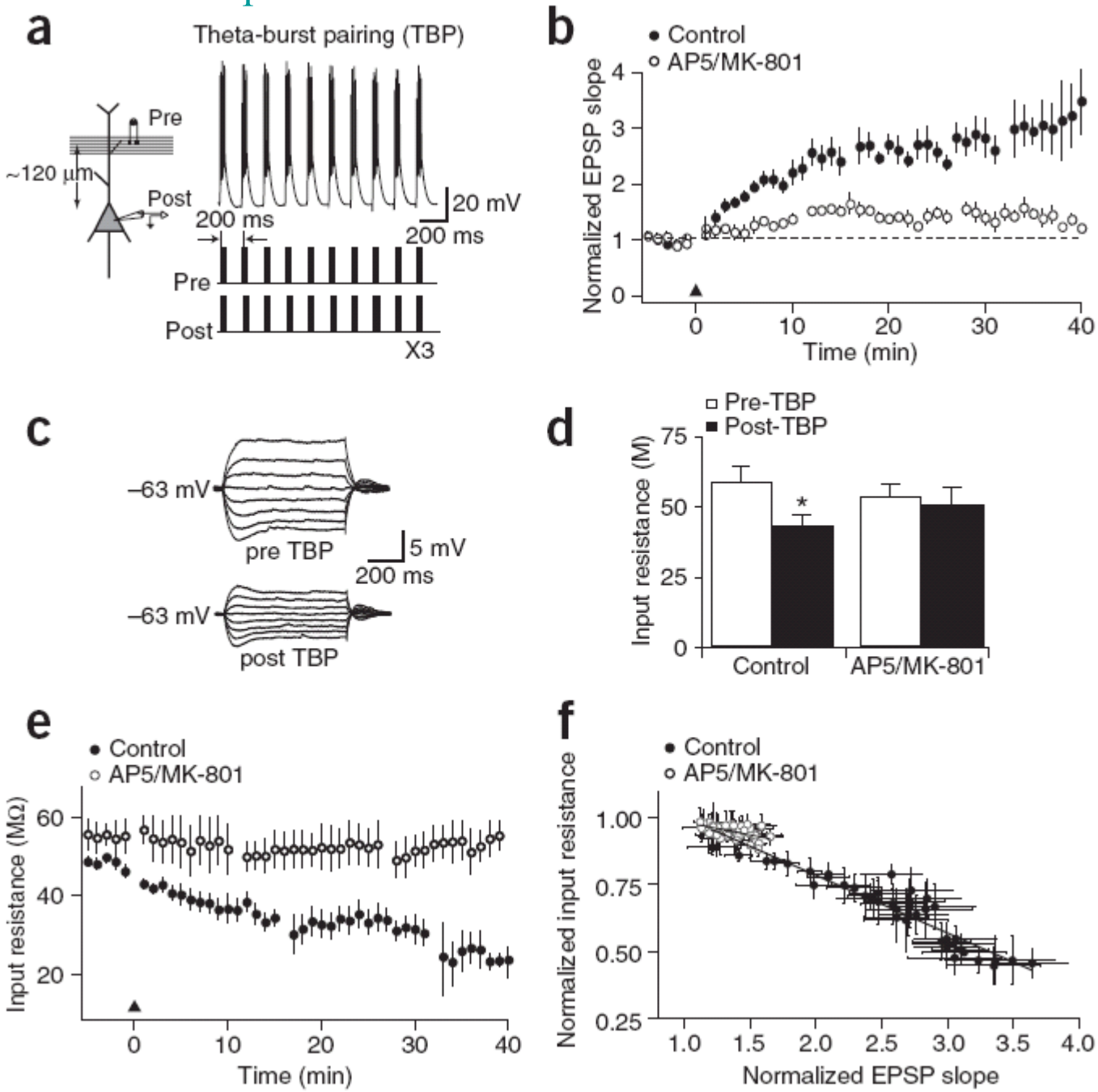
Somatic I injection



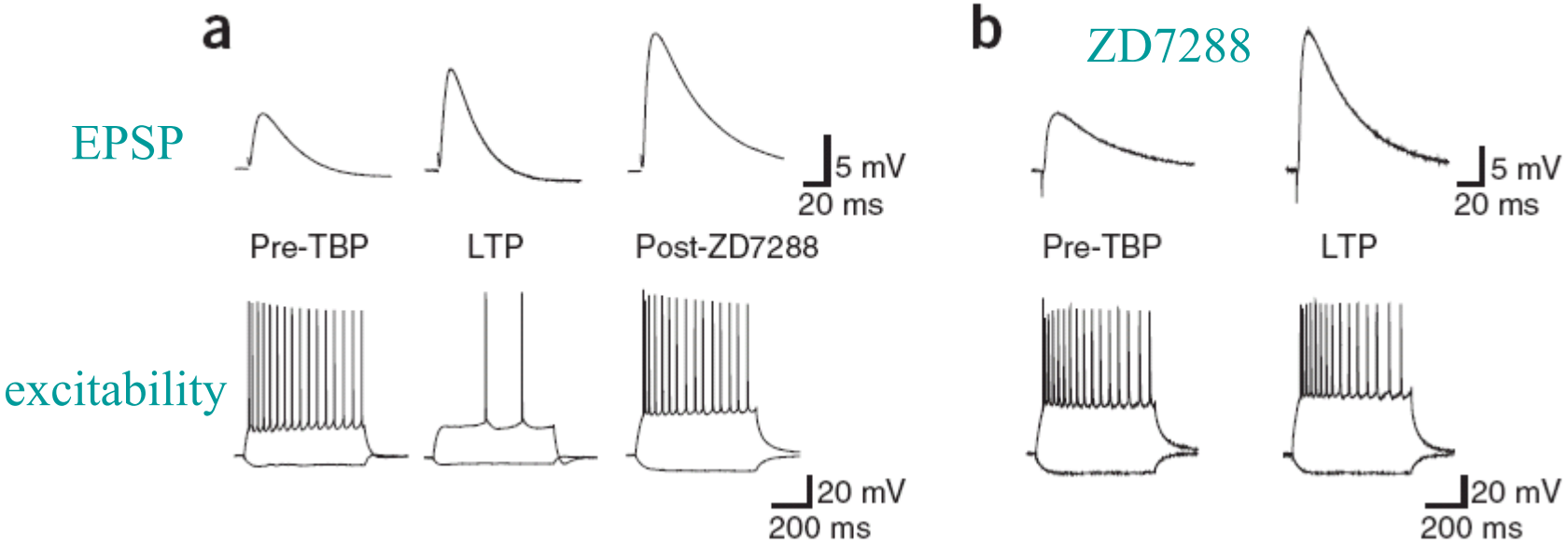

a
Ctrl
LTG
Both
5 mV
100 ms
b
Ctrl
ZD
Both
5 mV
100 ms


a
-45
V_c
-75 mV
-85 mV
-95 mV
-105 mV
-115 mV
-125 mV
10 pA
250 ms
b
-45
-115 mV
Soma
Dendrite
10 pA
250 ms
c
1.0
0.8
0.6
0.4
0.2
0.0
I/I_{max}
LTG
Ctrl
-120
-100
-80
-60
-40
V (mV)
d
-45
-64 mV
Ctrl
LTG
10 pA
250 ms

CA1 Schaffer-collateral inputs



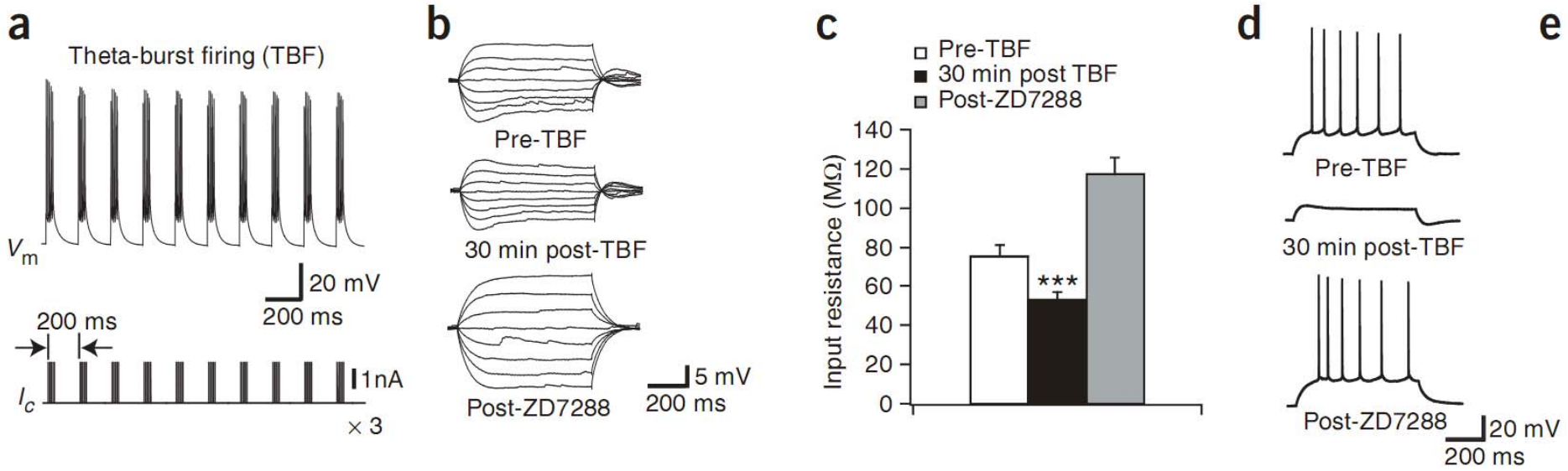
Although I_h ↑ after LTP induction, blocking I_h doesn't inhibit LTP.



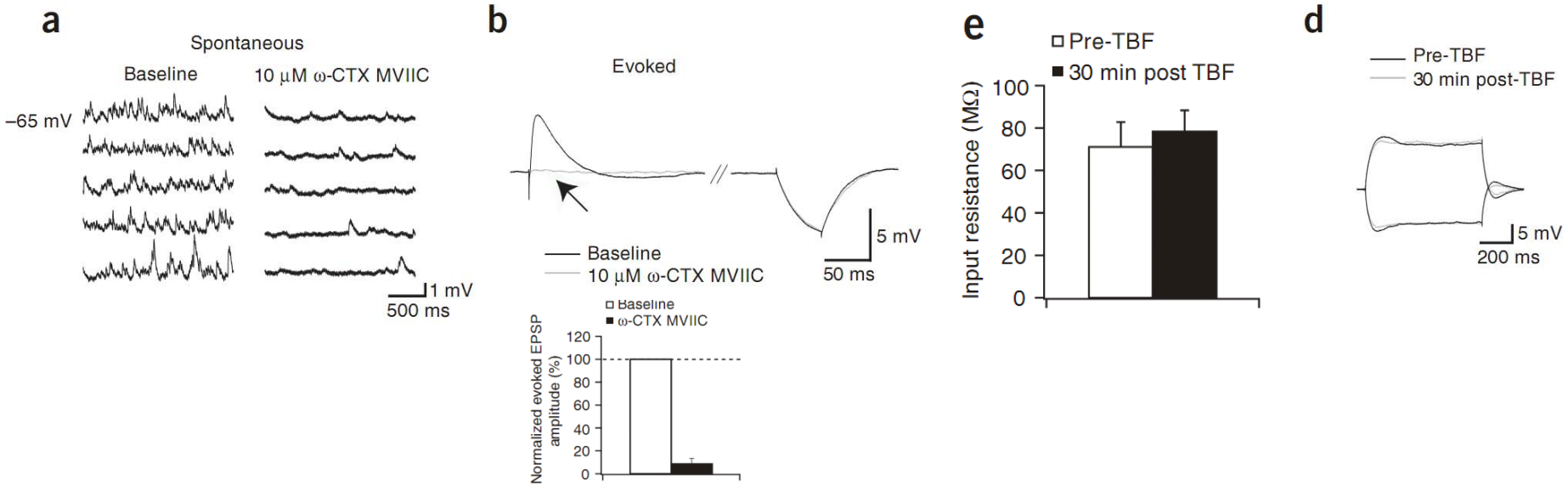
Nat Neurosci. 2005 Nov;8(11):1542-51

theta burst

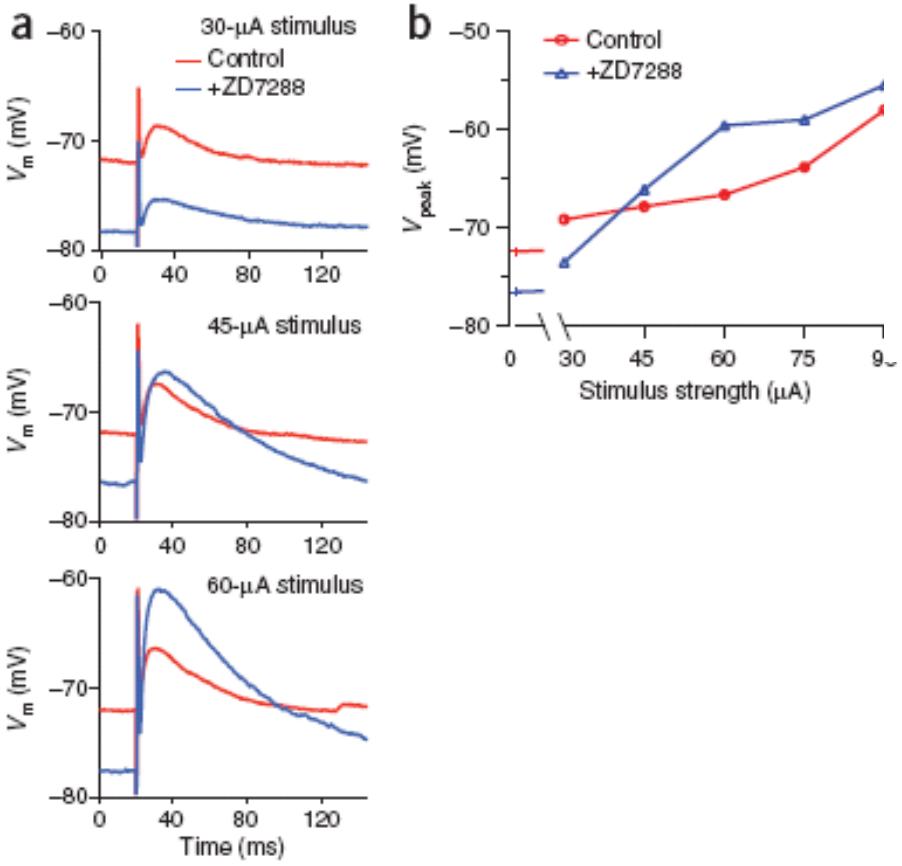
Postsynaptic TBF alone is sufficient to ↑I_h and ↓ R_{in}. No Need for pairing w/ synaptic inputs.

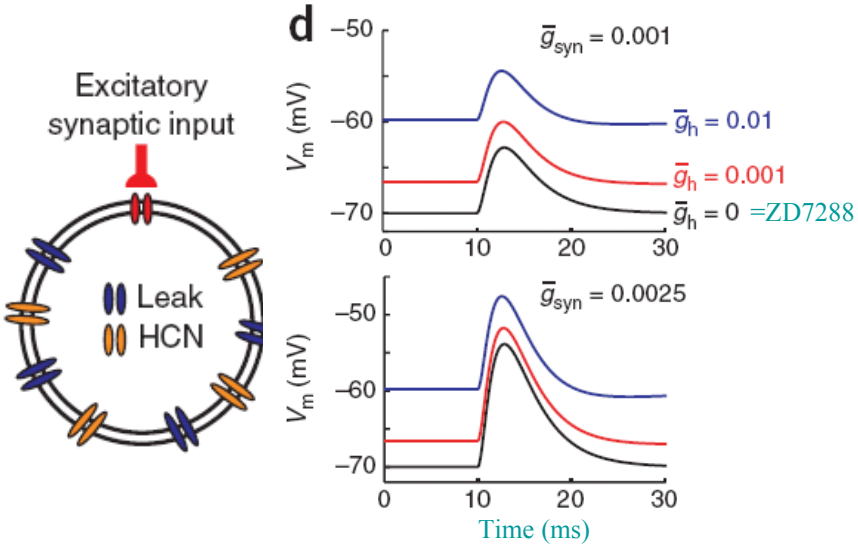


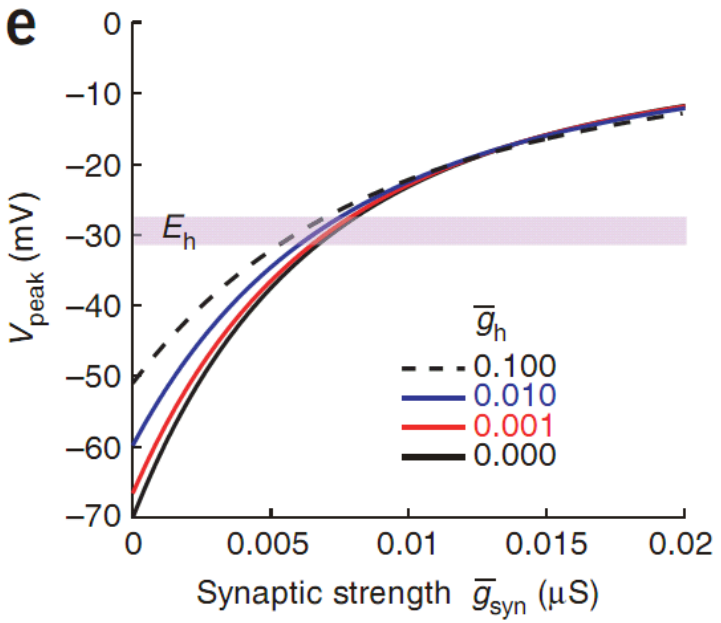
However, if there is no synaptic, glutamiergic, input, TBF cannot ↑I_h and ↓ R_{in}.
I_h ↑ is mediated through NMDA/Ca^{2+} CAMKII pathway.



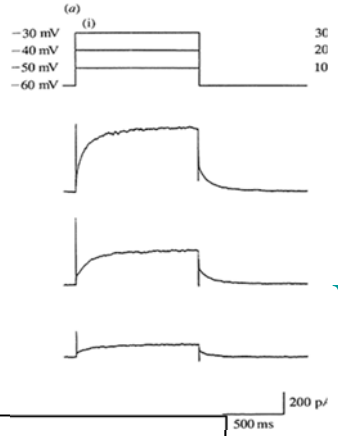
No strong inhibitory effect in a model containing I_h alone.



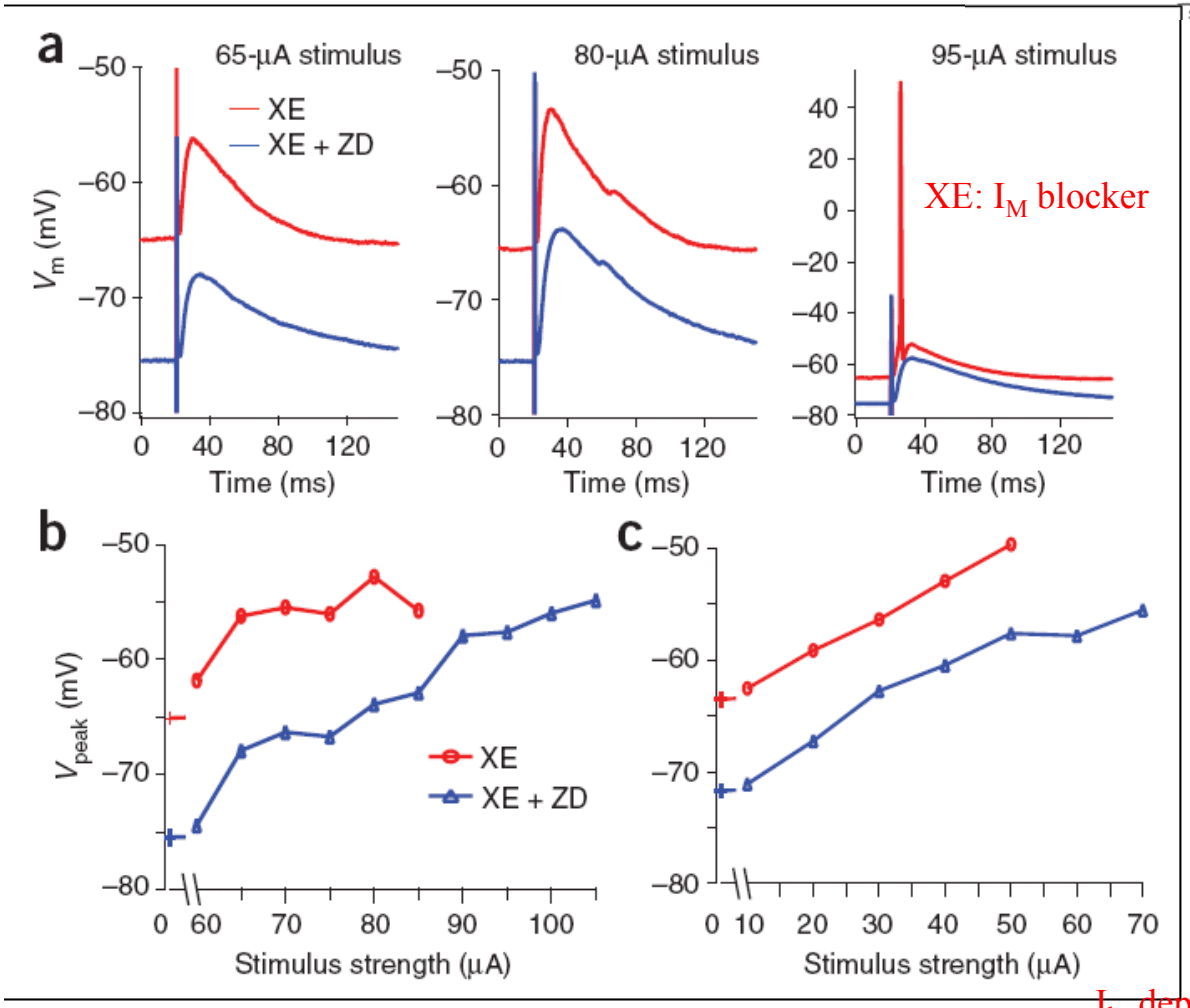


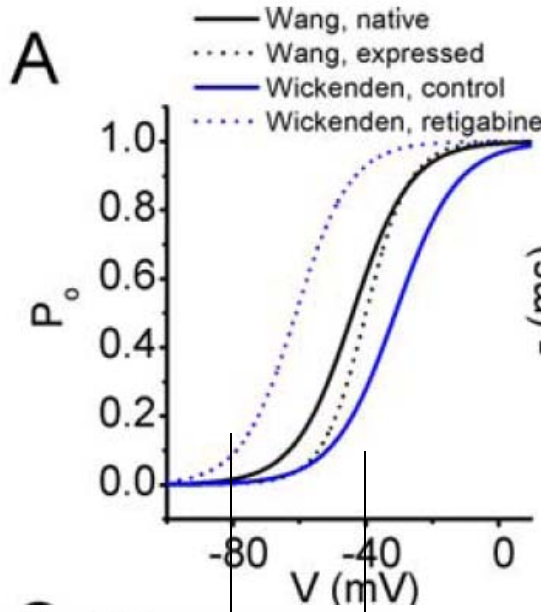


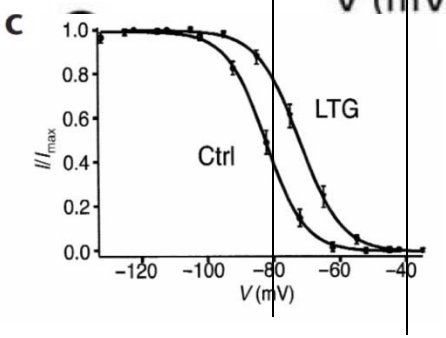
George, M.S., Abbott, L.F. & Siegelbaum, S.A. *Nat. Neurosci.* **12**, 577–584 (2009).



V range of I_M activation.



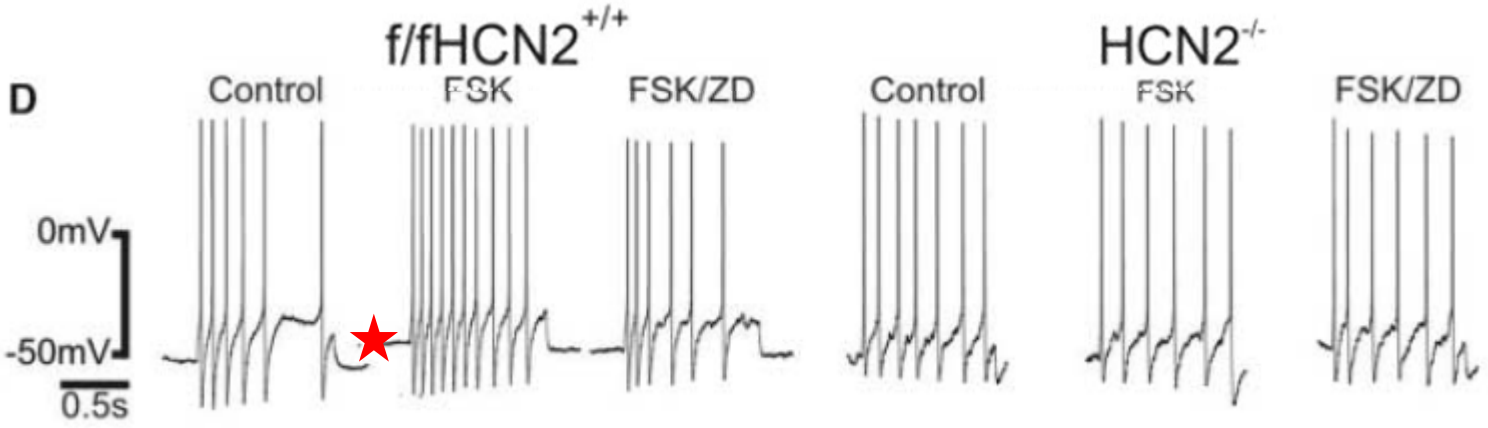




V range of I_h activation.

I_h depol. V_m, turning on I_M ➔ net inhibitory effect.

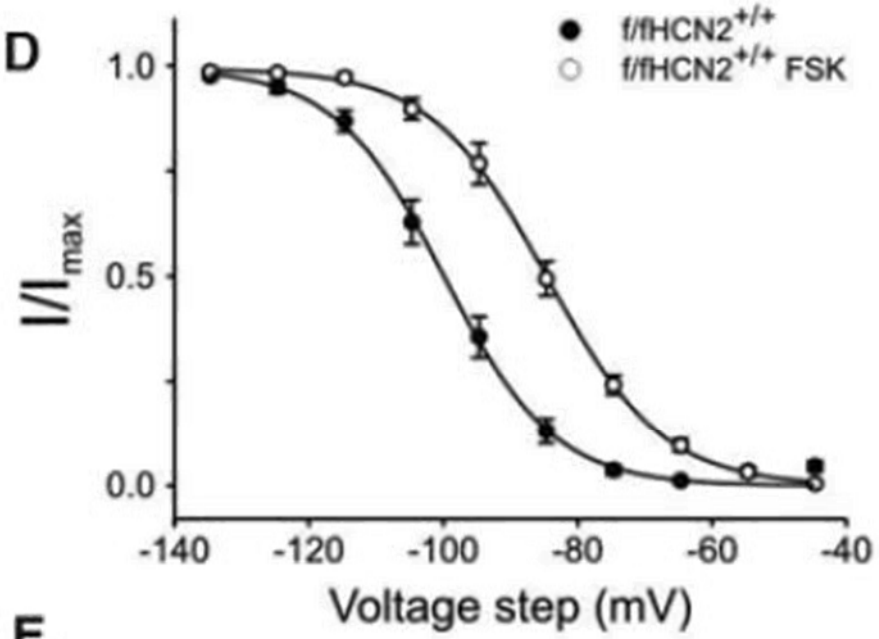
Firing in DRG neurons mediating pain.

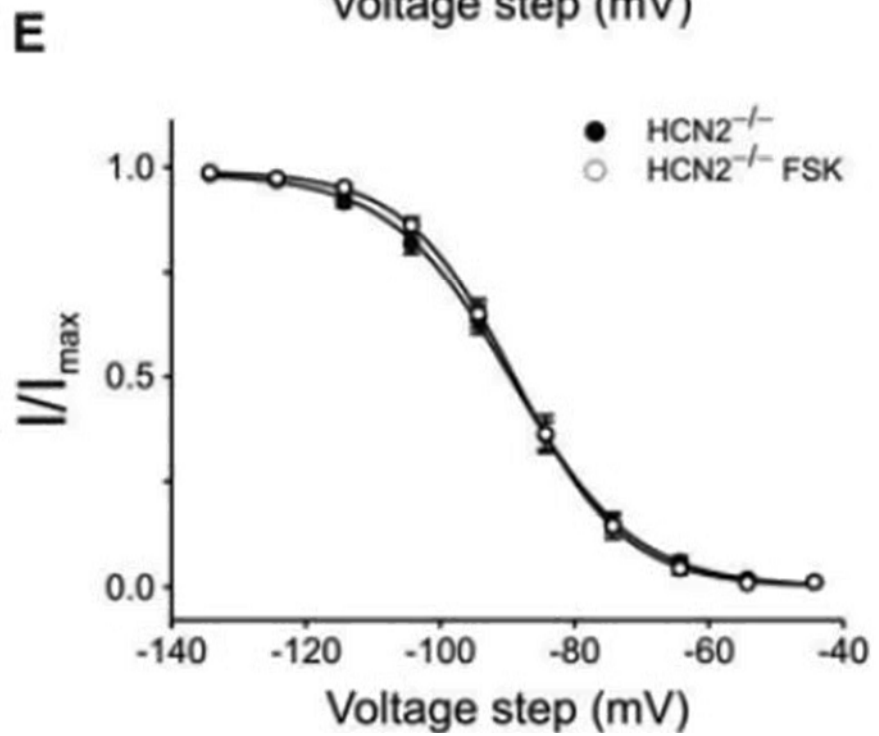


FSK (Forskolin): directly stimulates adenylate cyclase (AC)

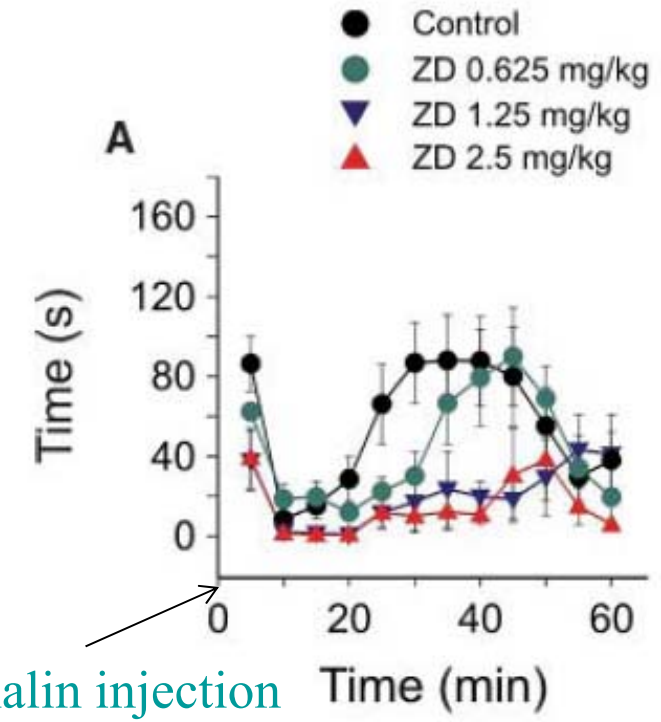
Science **333**, 1462 (2011)

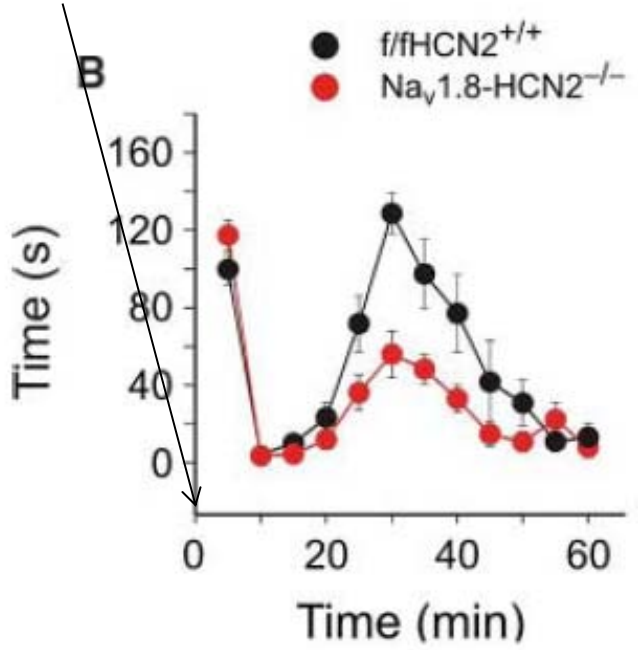
I_h in DRG neurons mediating pain sensitivity.





Formalin injection





Vaidya SP & Johnston D (2013). Temporal synchrony and gamma-to-theta power conversion in the dendrites of CA1 pyramidal neurons. *Nat Neurosci* **16**, 1812–1820

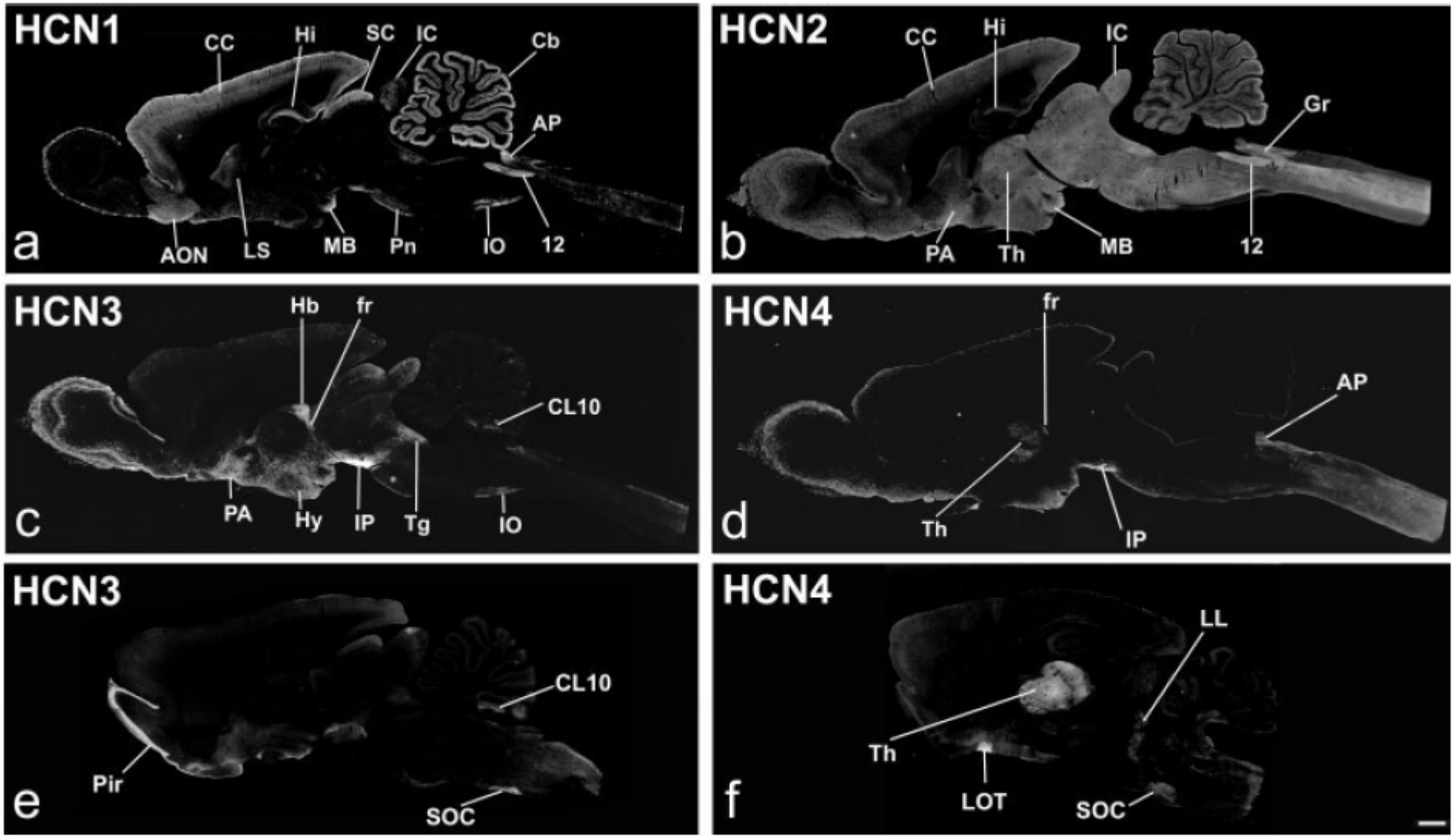
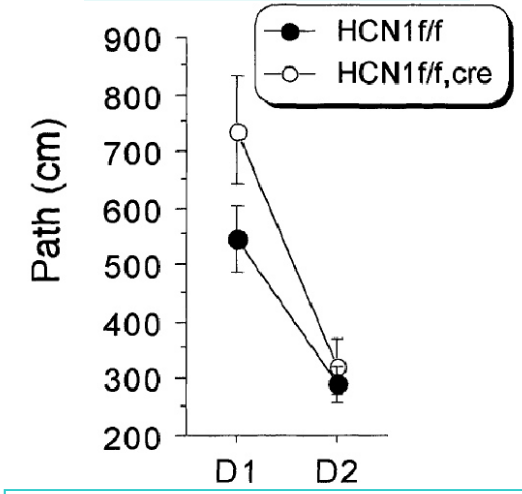


Fig. 3. Distribution of immunoreactivity for HCNs in the rat brain. Parasagittal sections of the rat brain were immunostained with HCN1 (**a**), HCN2 (**b**), HCN3 (**c**,**e**), and HCN4 (**d**,**f**) antibodies. 12, hypoglossal nucleus; AON, anterior olfactory nuclei; AP, area postrema; Cb, cerebellar cortex; CC, cerebral cortex; CL10, cerebellar cortex lobule 10; fr, fasciculus retroflexus; Gr, gracile nucleus; Hb, habenular nucleus; Hy, hypothalamus; Hi, hippocampus; IC, inferior colliculus; IO, inferior olive; IP, interpeduncular nucleus; LOT, nucleus of the lateral olfactory tract; LL, lateral lemniscus; LS, lateral septum nucleus; MB, mammillary body; PA, preoptic area; Pir, piriform cortex; Pn, pontine nuclei; SC, superior colliculus; SOC, superior olivary complex; Tg, tegmental nuclei; Th, thalamus. Scale bar = 1 mm.

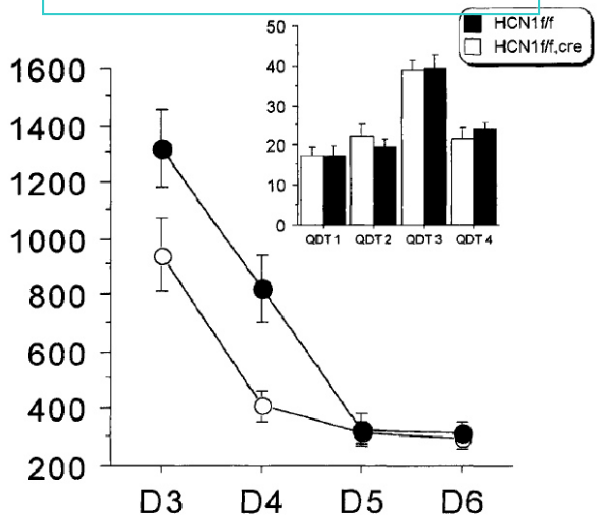
A

Flag submerged



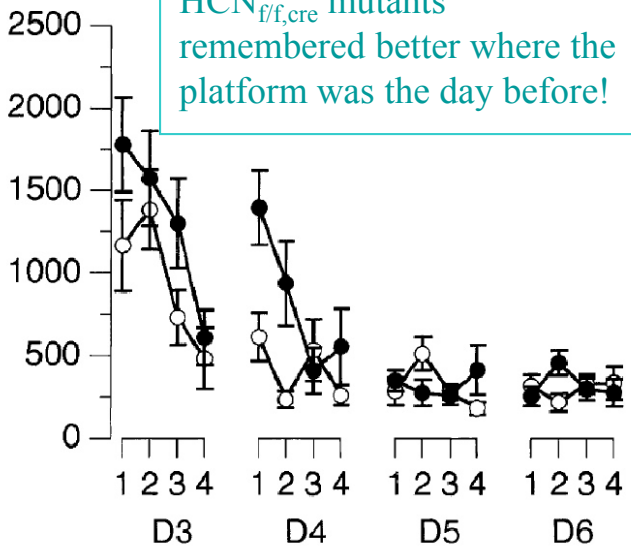
B

No flag, submerged 4 trial/day



C

On the 1st trial of day 3, $HCN_{f/f,cre}$ mutants remembered better where the platform was the day before!

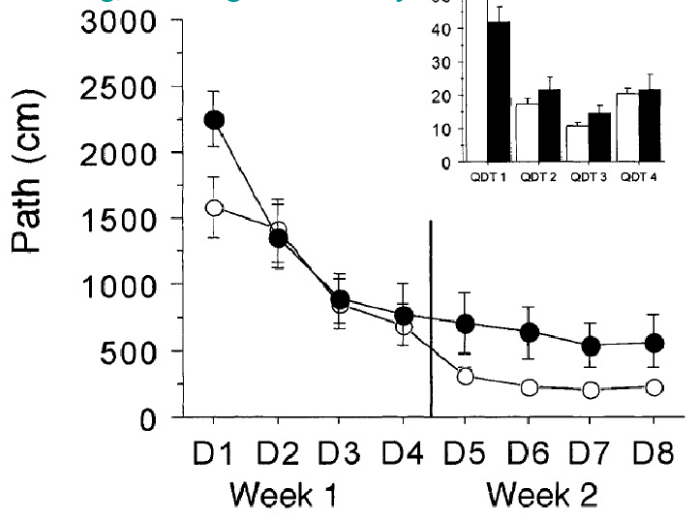


f/f: control
f/f,cre: HCN1 deleted in forebrain

Priming: animals placed on the platform for 15 sec 15 min before trial.
Early enhancement disappears w/o priming

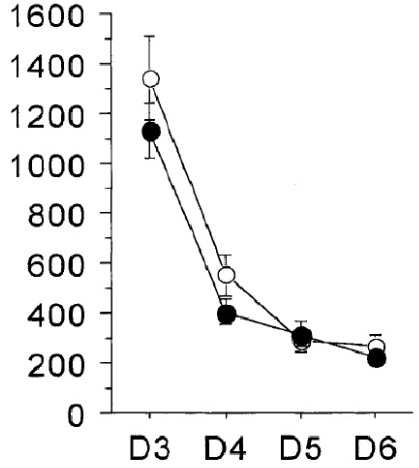
D

No flag, submerged 1 trial/day



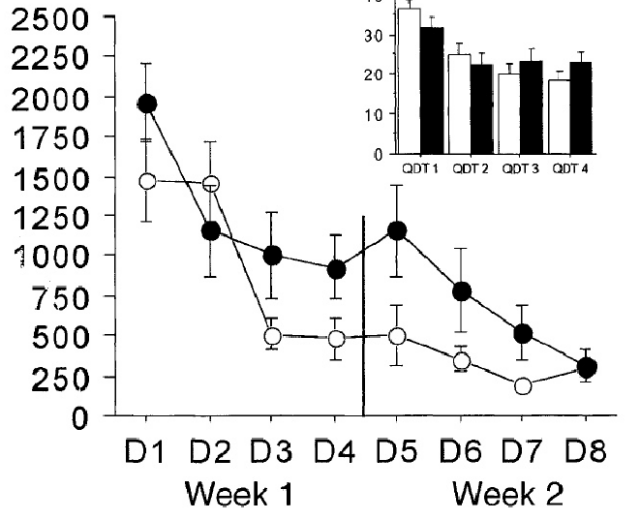
E

No priming
No flag, submerged 4 trial/day

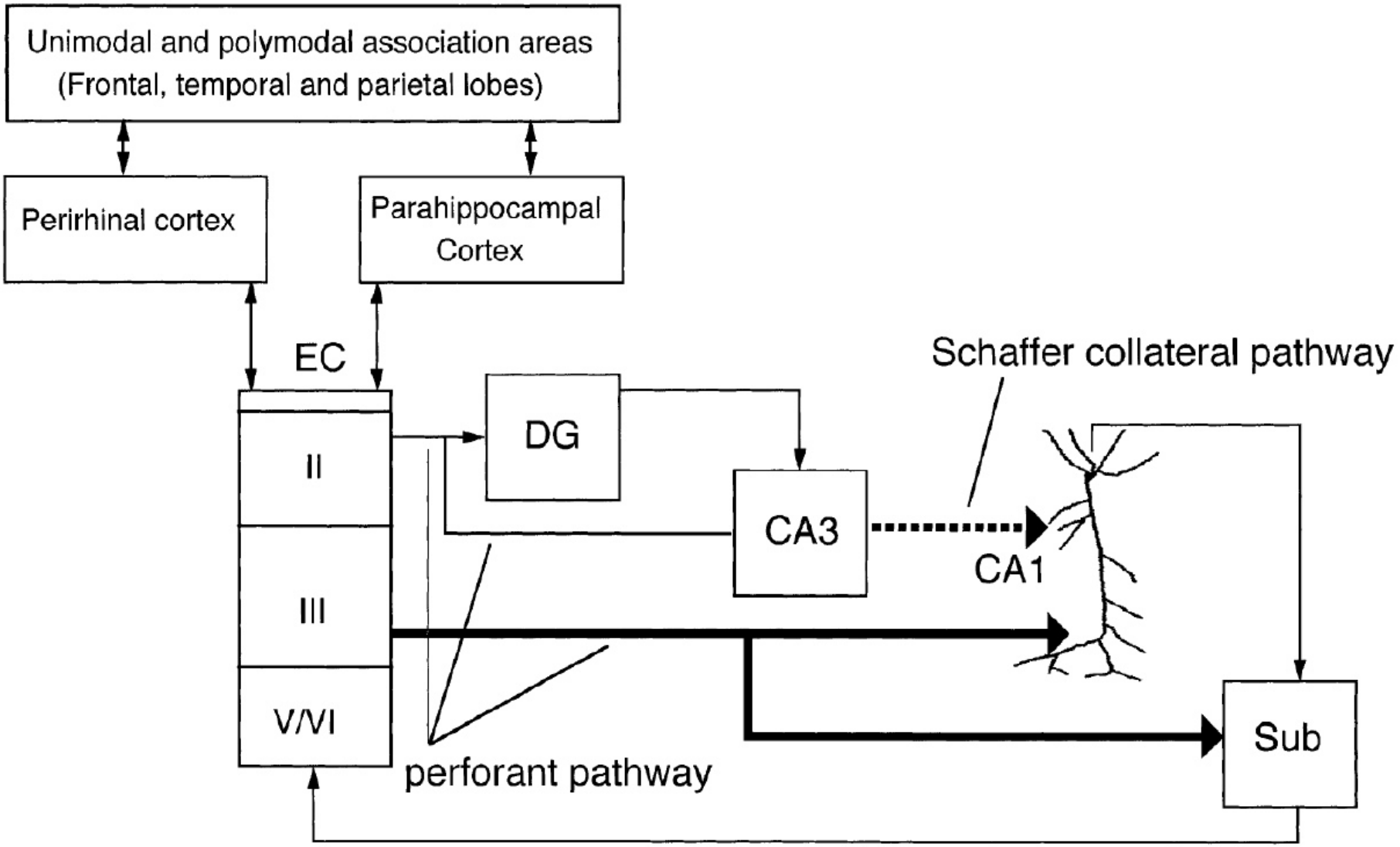


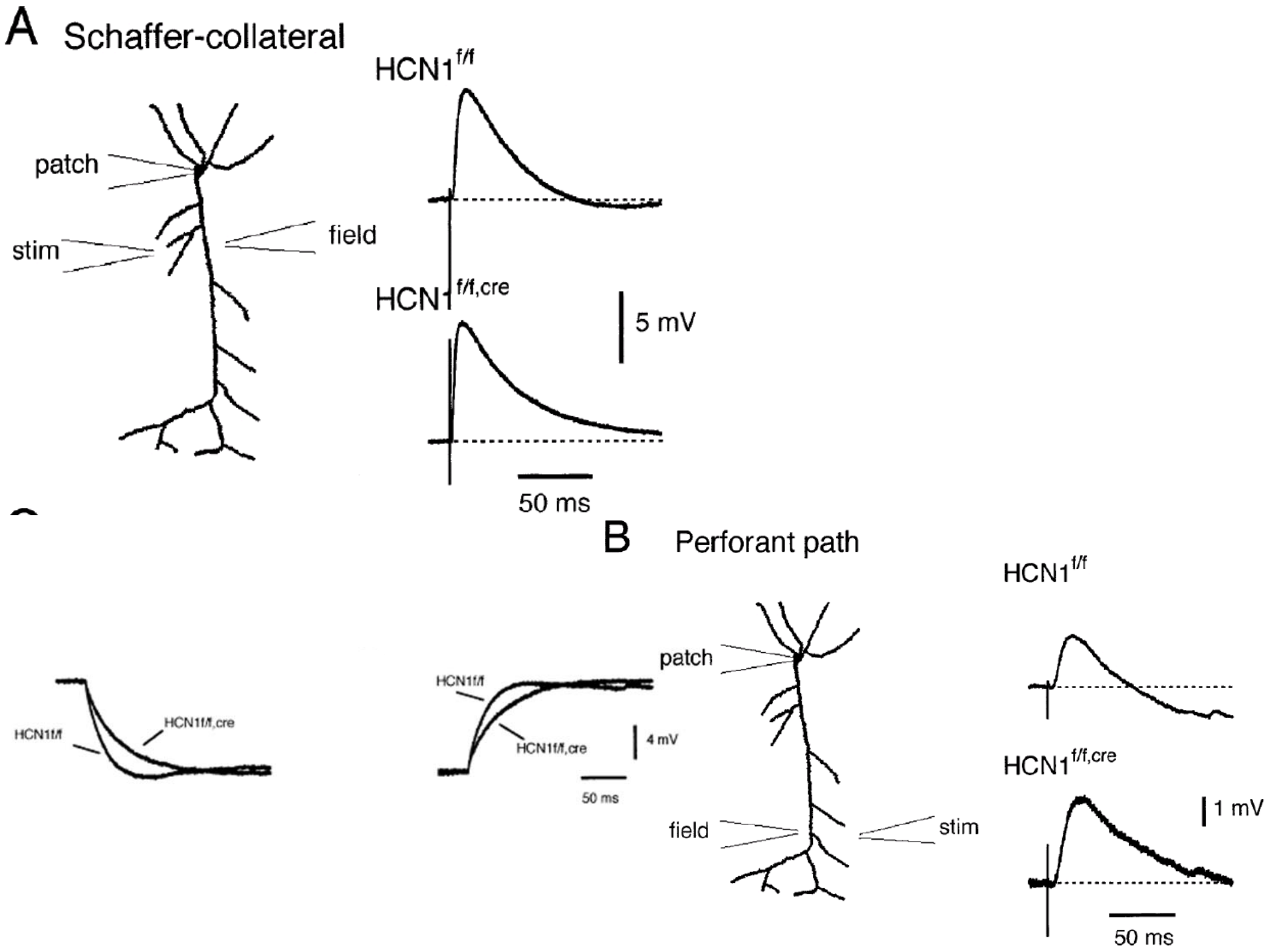
F

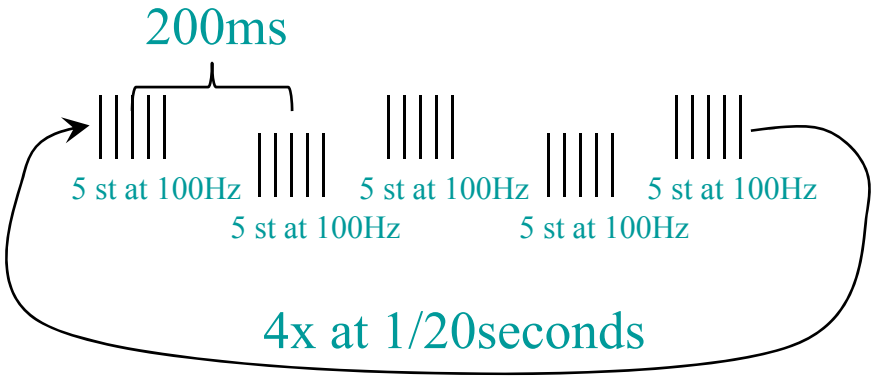
No priming
No flag, submerged 1 trial/day



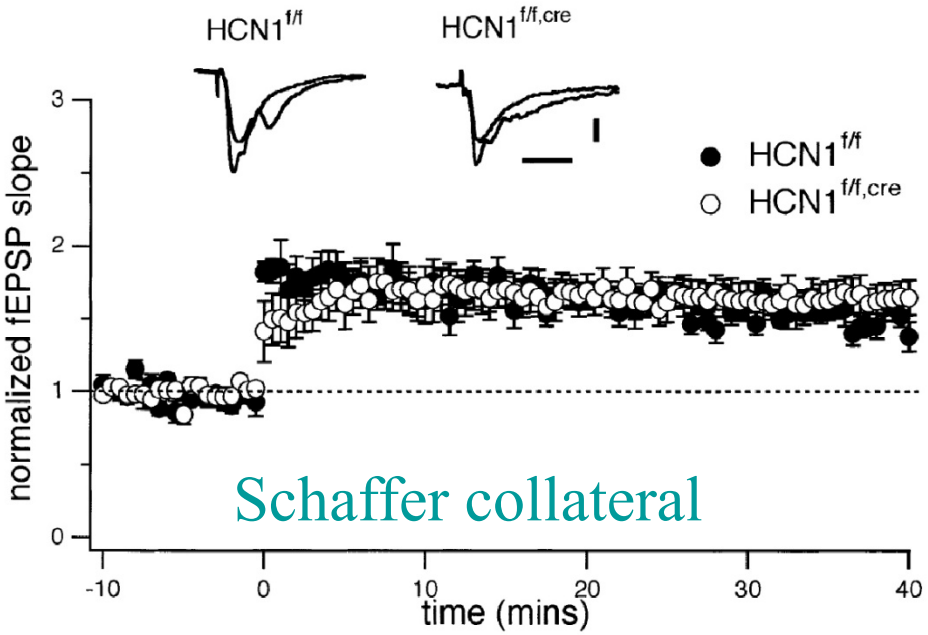
Delta wave (during sleep): ok
Theta wave (important for spatial learning and memory): enhanced.




A
Schaffer-collateral
patch
stim
field
HCN1f/f
HCN1f/f,cre
5 mV
50 ms
B
Perforant path
HCN1f/f
HCN1f/f,cre
4 mV
50 ms
patch
field
stim
HCN1f/f
HCN1f/f,cre
1 mV
50 ms



A



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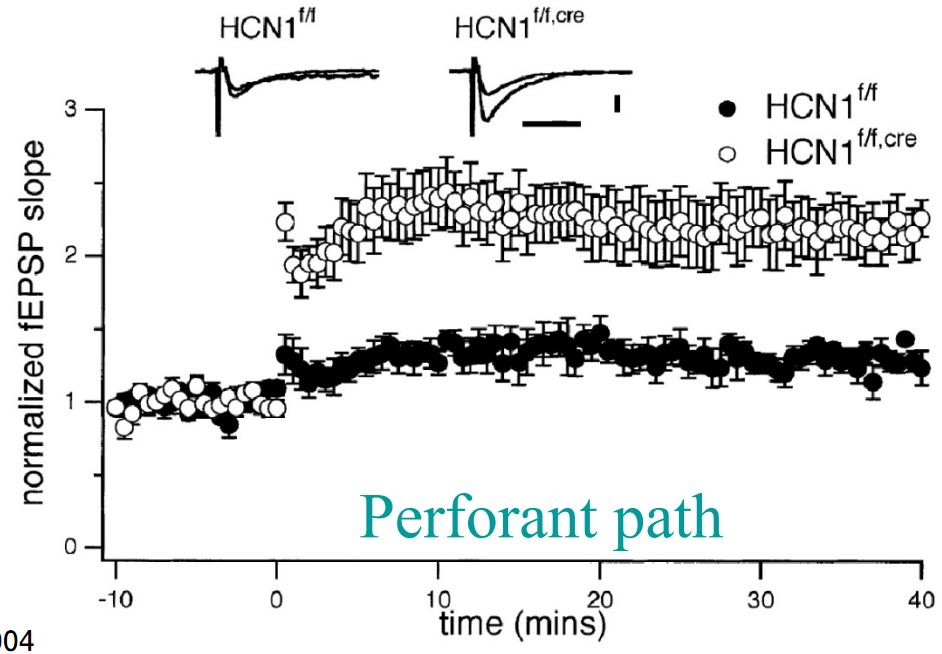

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Atherton JF, Kitano K, Baufreton J, Fan K,Wokosin D, Tkatch T, Shigemoto R, Surmeier DJ & Bevan MD (2010). Selective participation of somatodendritic HCN channels in inhibitory but not excitatory synaptic integration in neurons of the subthalamic nucleus. *J Neurosci* **30**, 16025–16040.