Synaptic Plasticity

"the only game in town"
-R. Malenka

Short Term Plasticity
- Paired pulse facilitation / depression
- Presynaptic modulation
- Presynaptic receptors
- Postsynaptic modulation

Long Term Plasticity
- LTP, LTD

Synapses vary!
Some important questions…

Synapses are modified in response to a wide range of stimuli, activity patterns, drugs, behavioral states, etc…

When changes in synaptic strength occur, what caused the change?

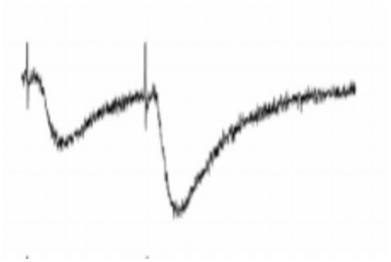
- …change in neurotransmitter release?
  - Mechanism?
- …change in postsynaptic sensitivity to neurotransmitter?
  - Mechanism?
- …change in synapse number?
  - Mechanism?

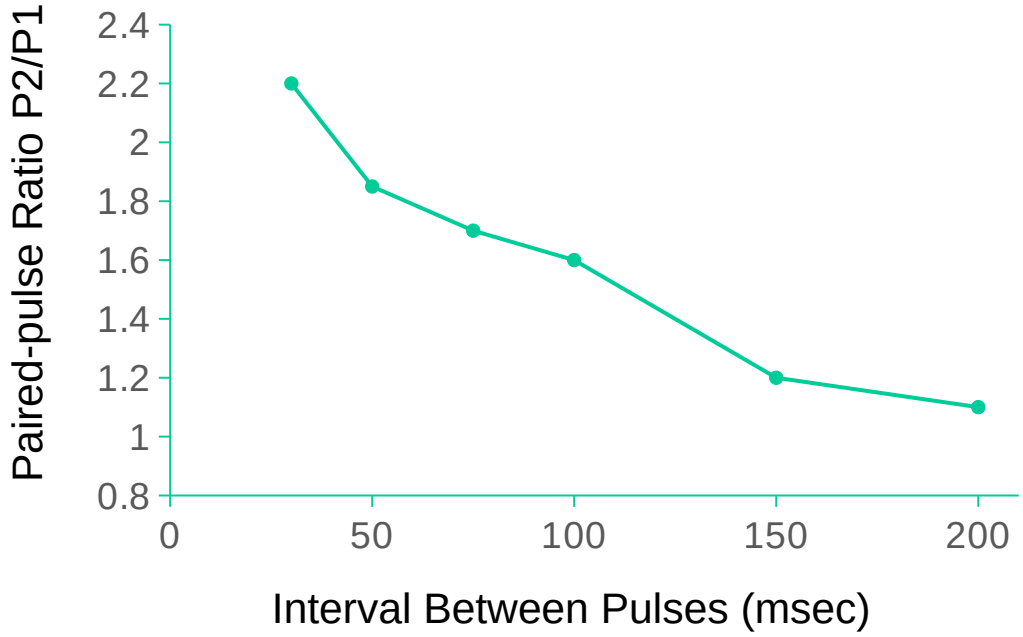
“Necessary”, “Sufficient”, “Mediator”, “Modulator”….

Paired Pulse Ratio

ISI = 50 msec

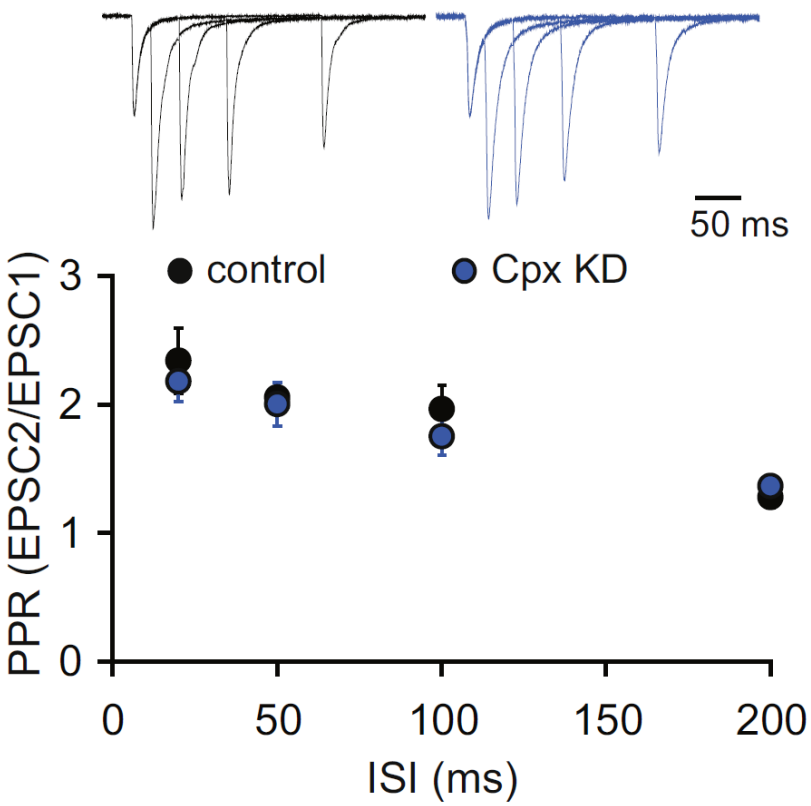
ISI = 200 msec





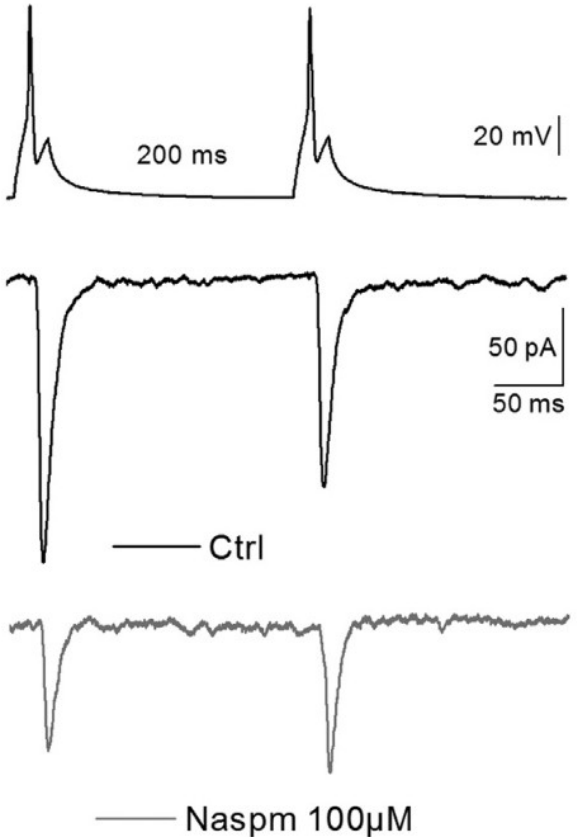
Paired Pulse Ratio

Facilitation



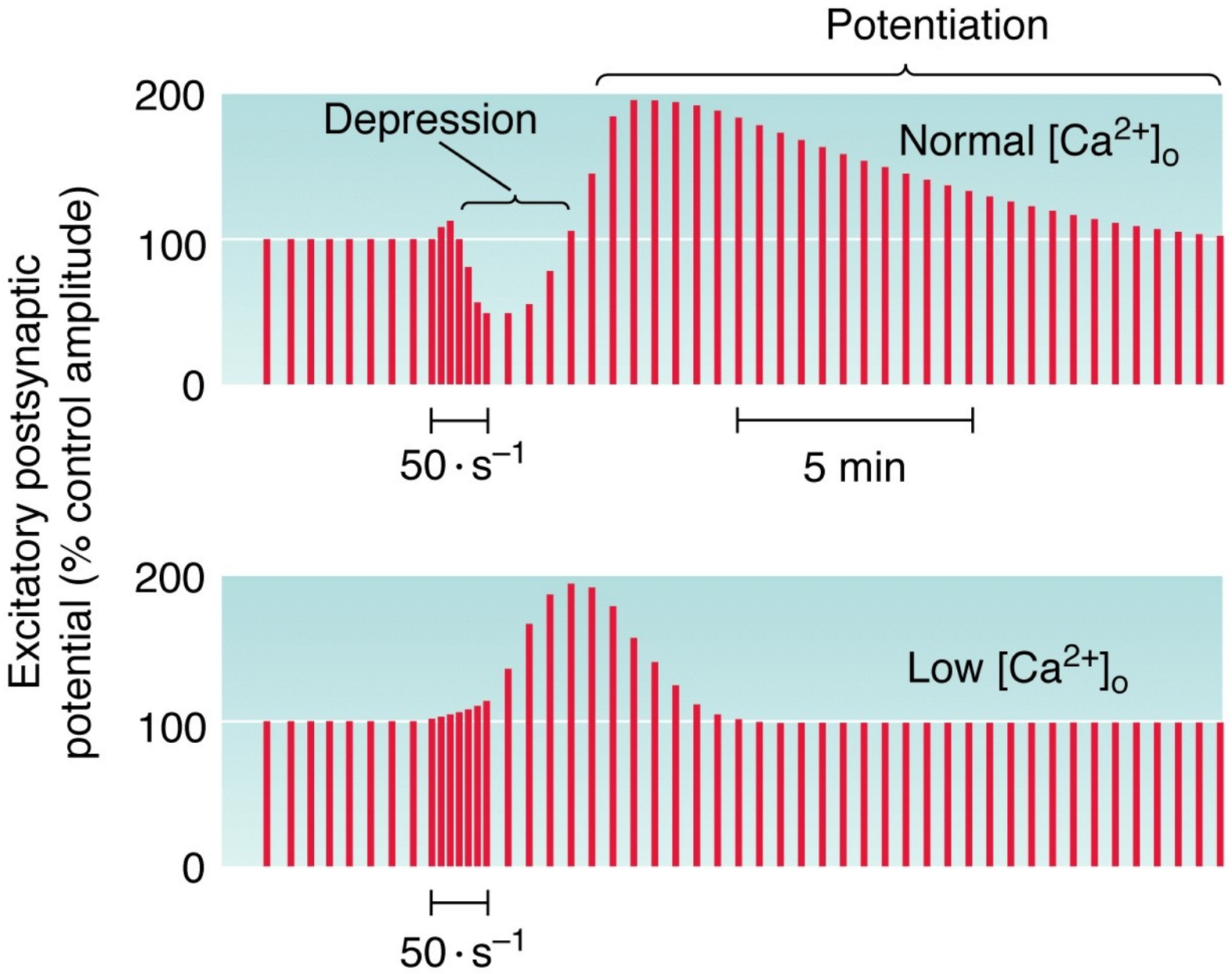
Ahmad et al 2012

Depression

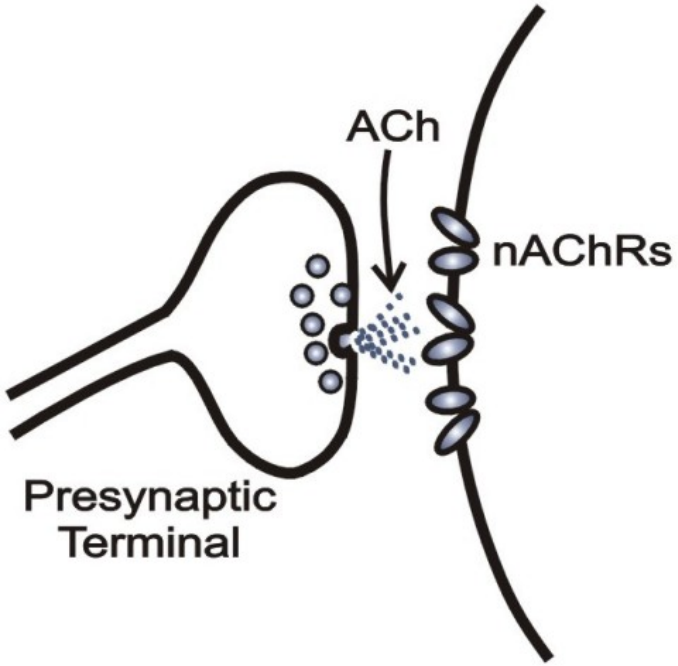


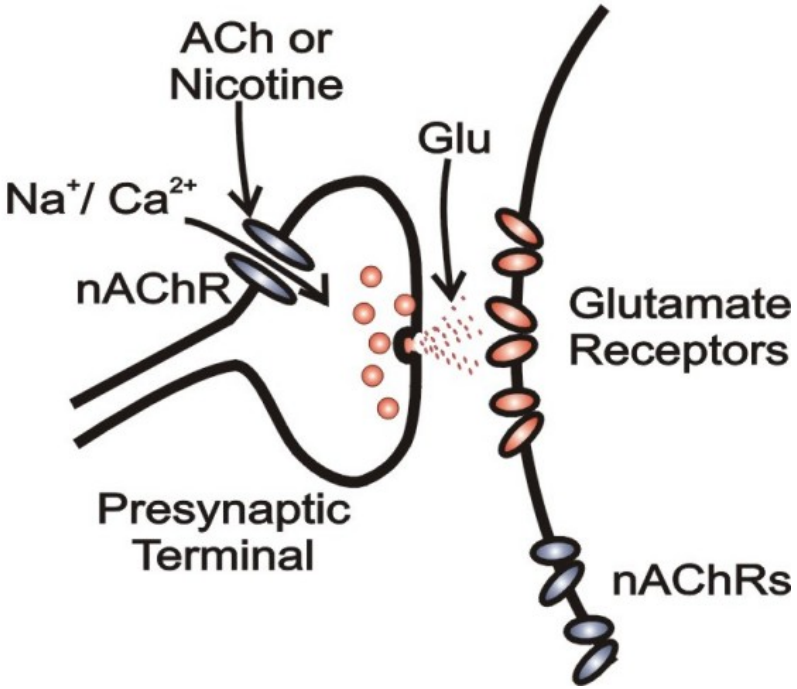
Shypshyna & Veselovsk 2015

Post-Tetanic Potentiation at the NMJ

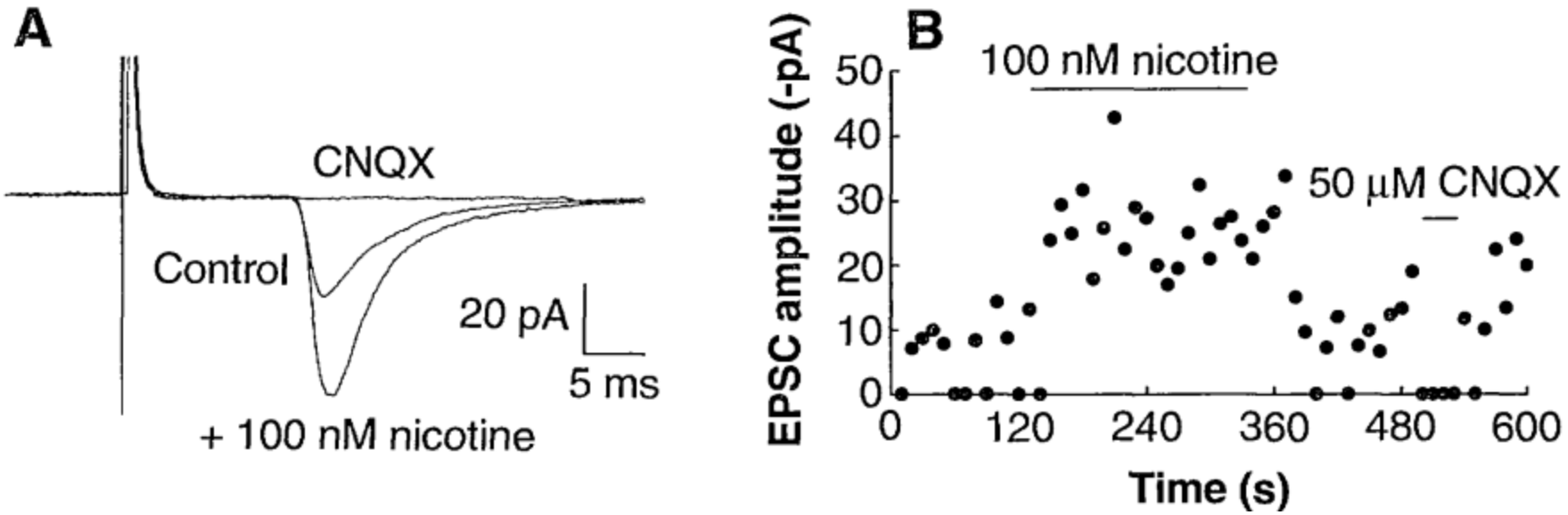


Modulation of Synaptic Strength via Presynaptic Receptors



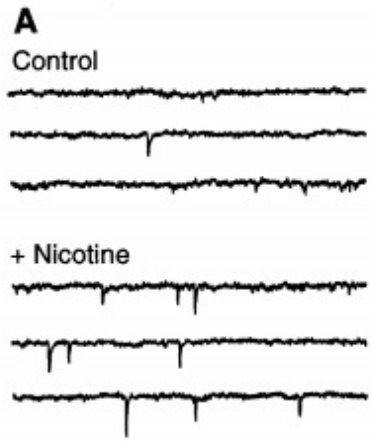


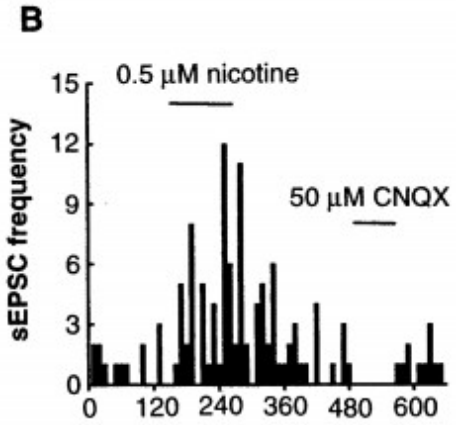
Nicotine Enhances Excitatory Synaptic Transmission

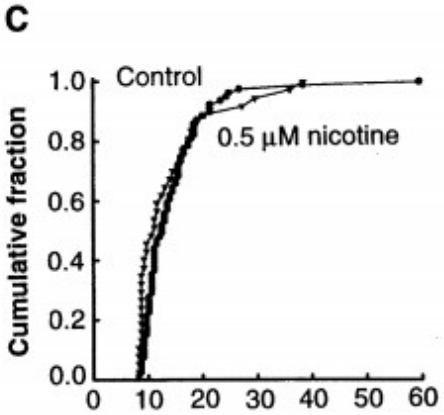


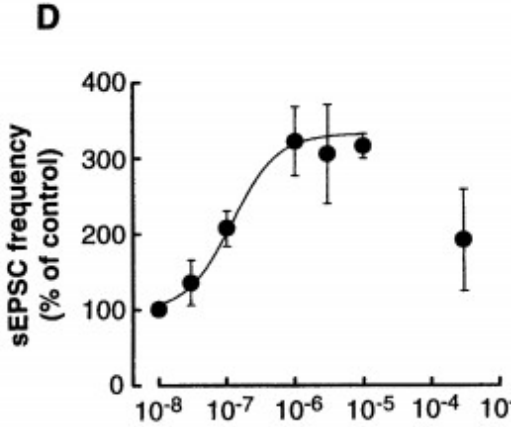
McGehee et al 1995

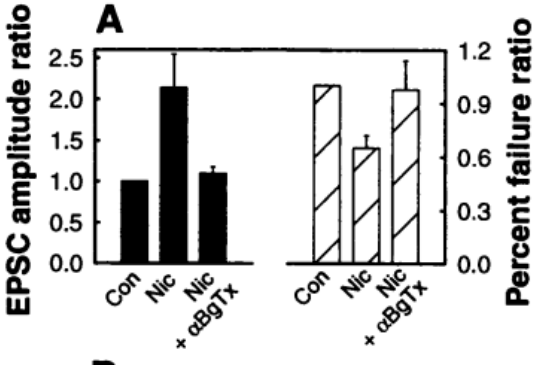
Nicotine Enhances Excitatory Synaptic Transmission via a7 nAChRs

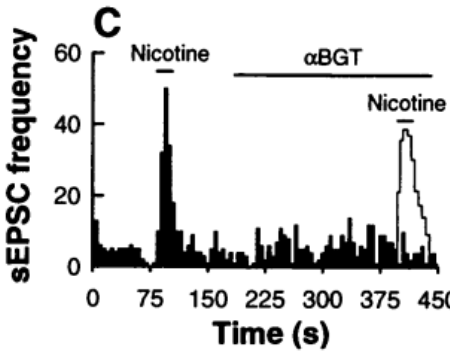


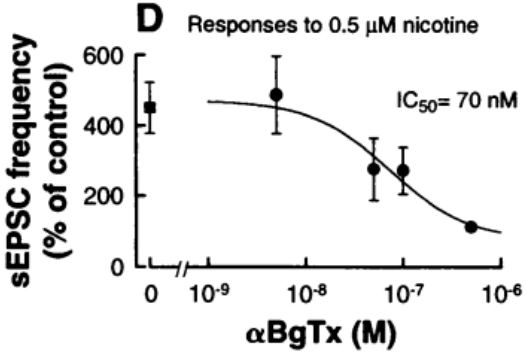






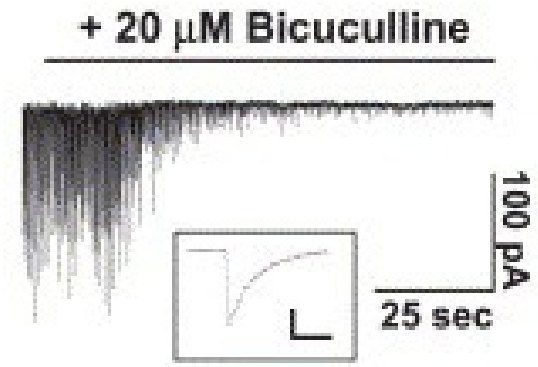


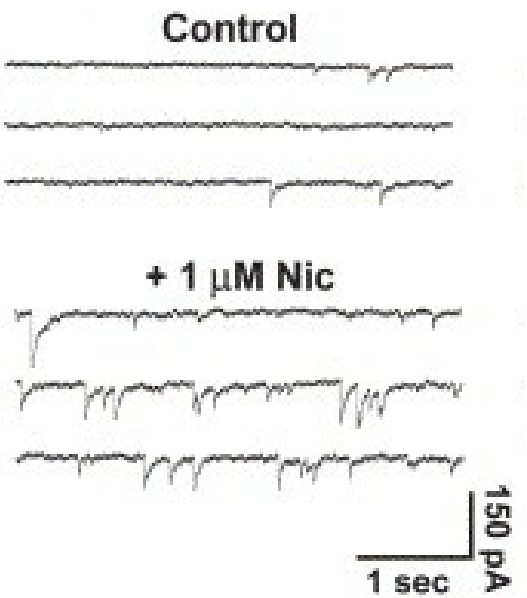


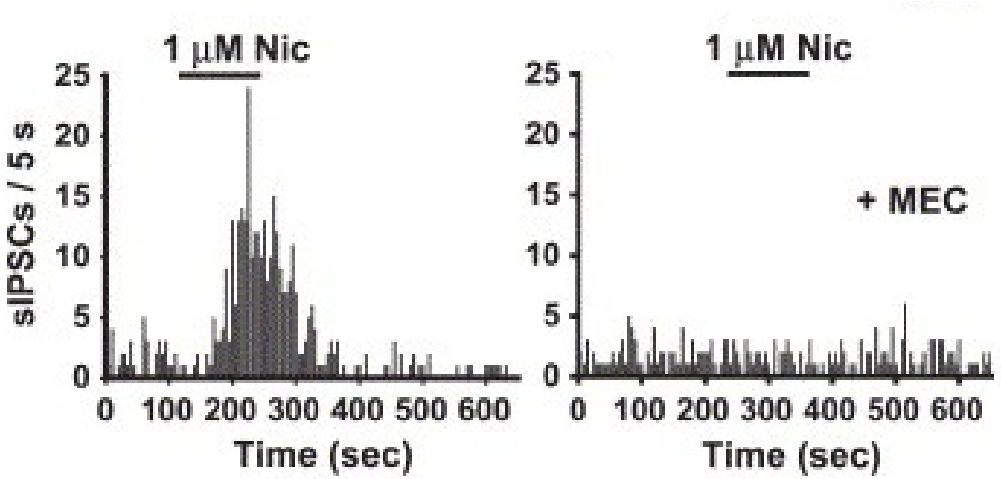


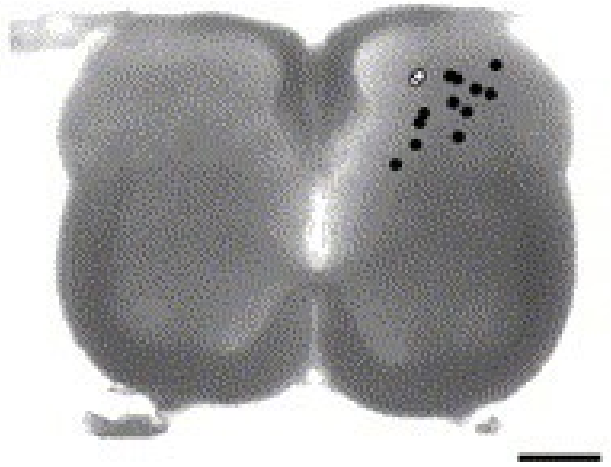
McGehee et al 1995

β2* nAChRs enhance inhibitory drive to spinal dorsal horn neurons



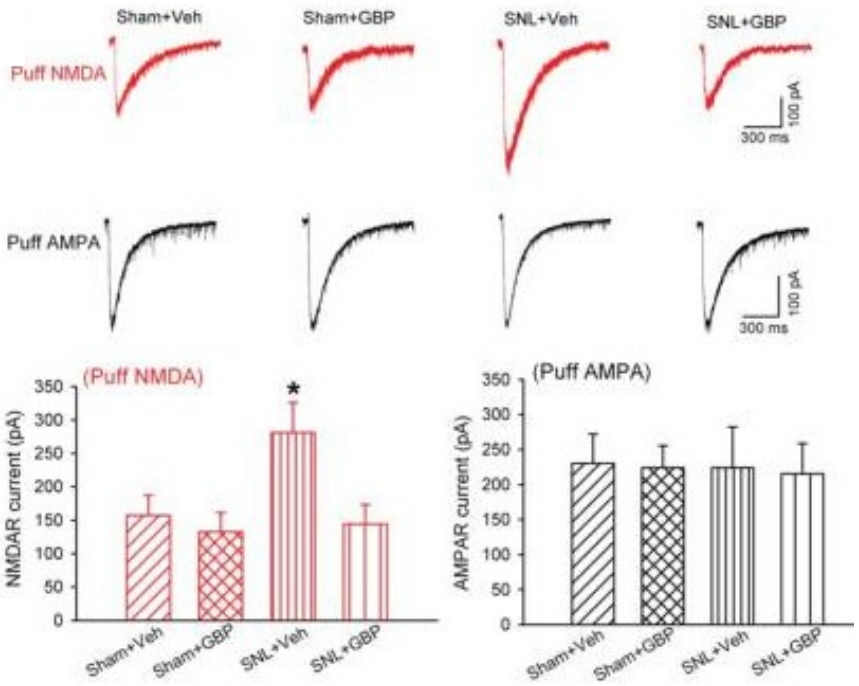


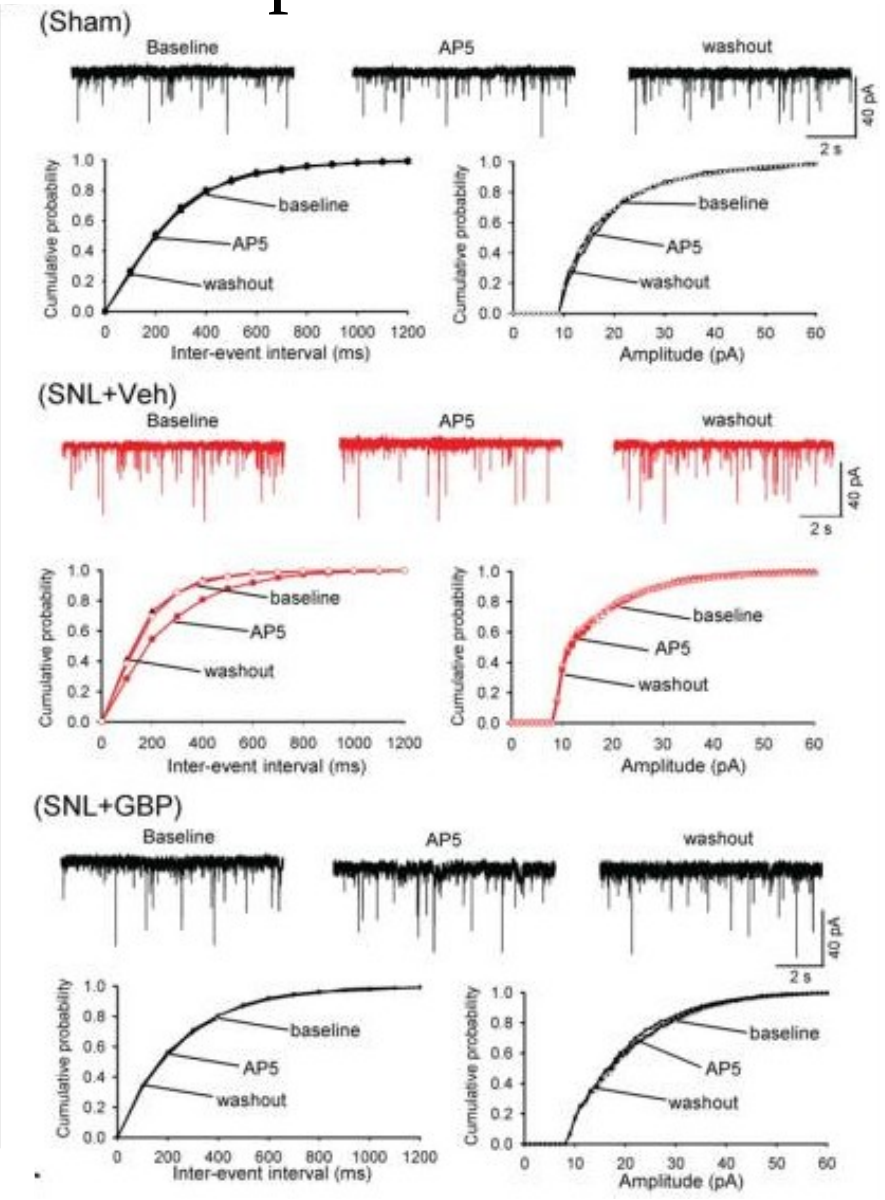




Genzen et al 2005

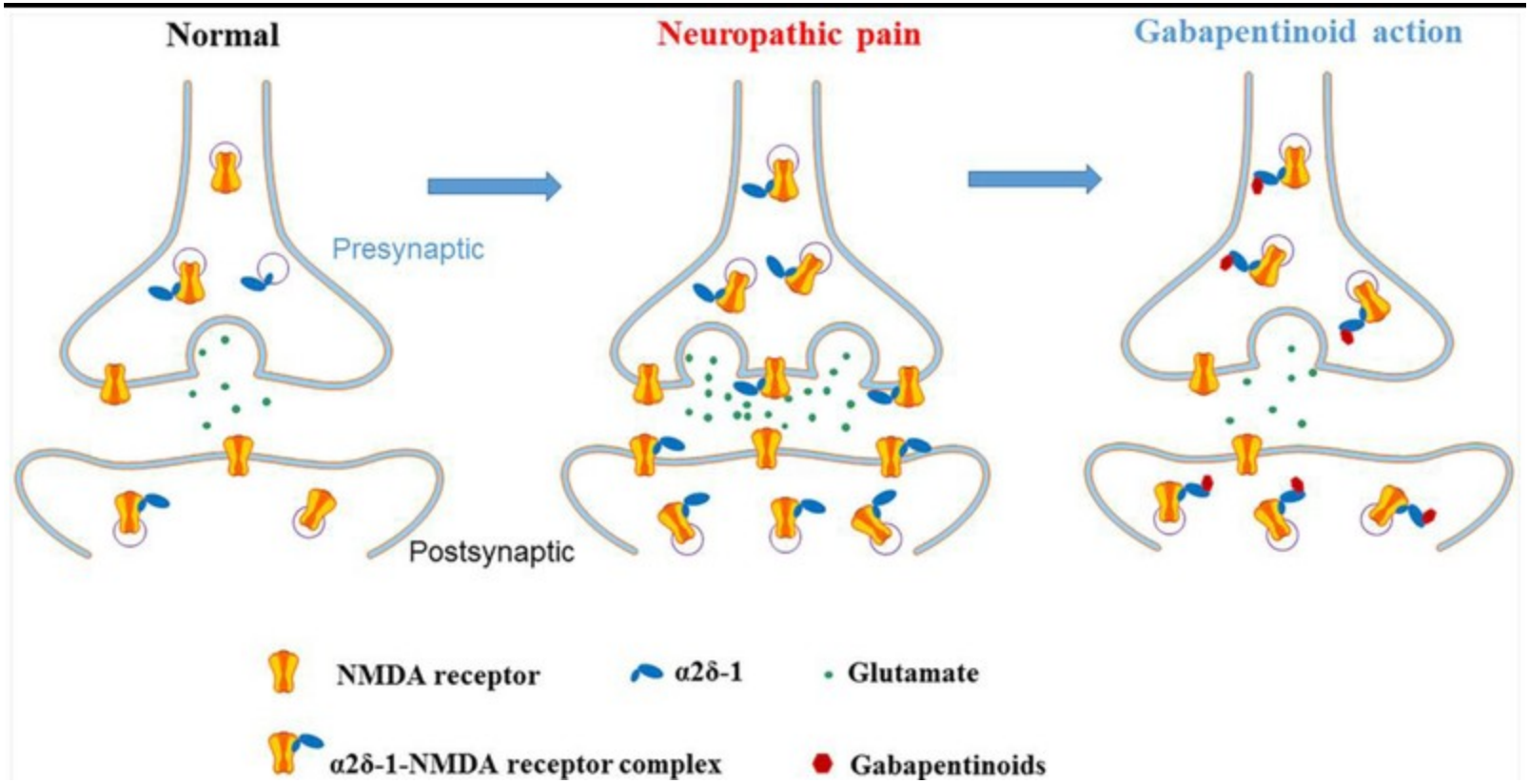
Presynaptic NMDA receptors in spinal cord are increased in a chronic pain state





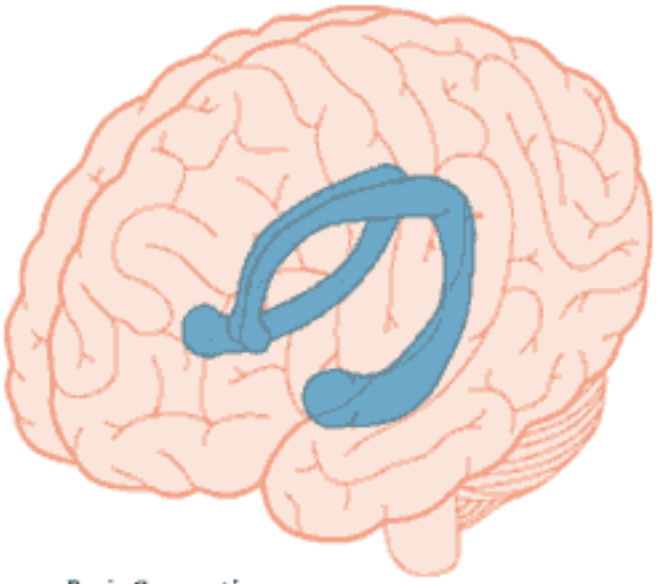
Deng et al., 2019

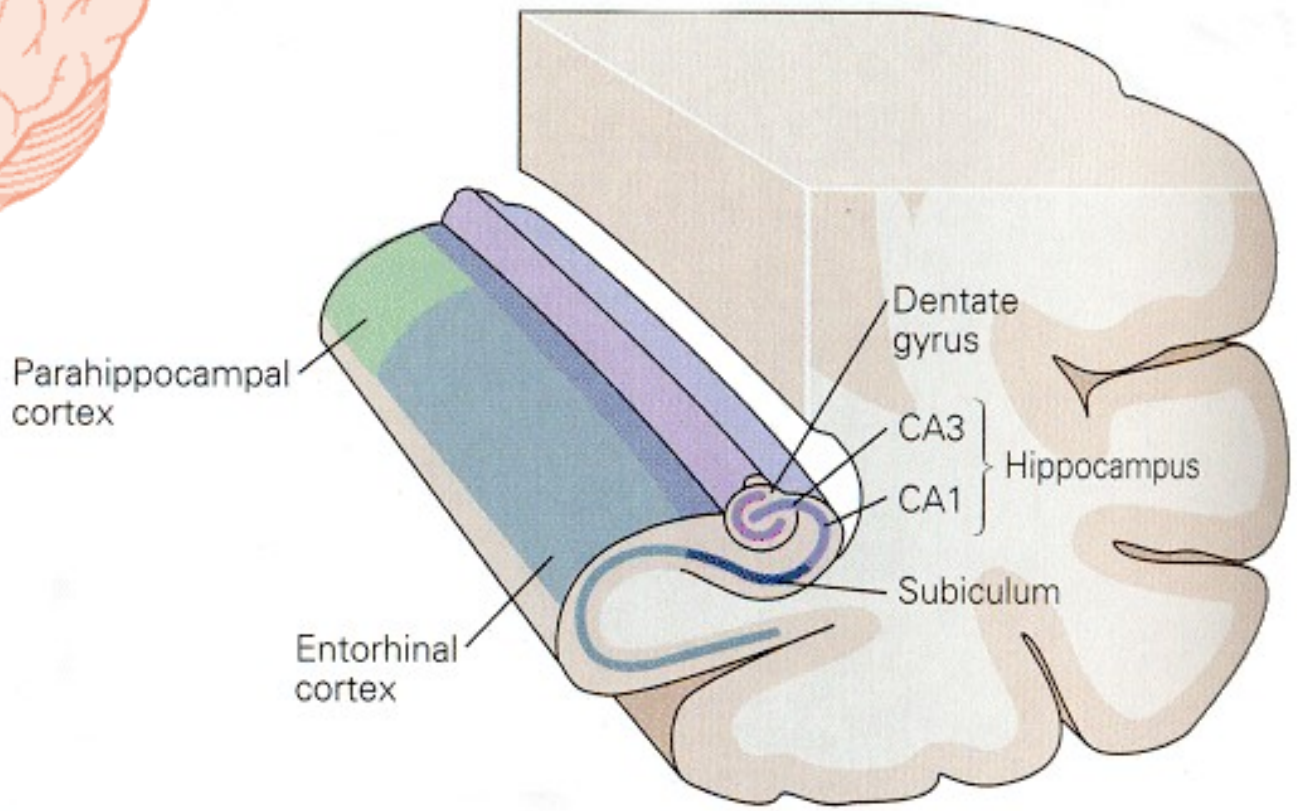
Presynaptic NMDA Receptors and Neuropathic Pain



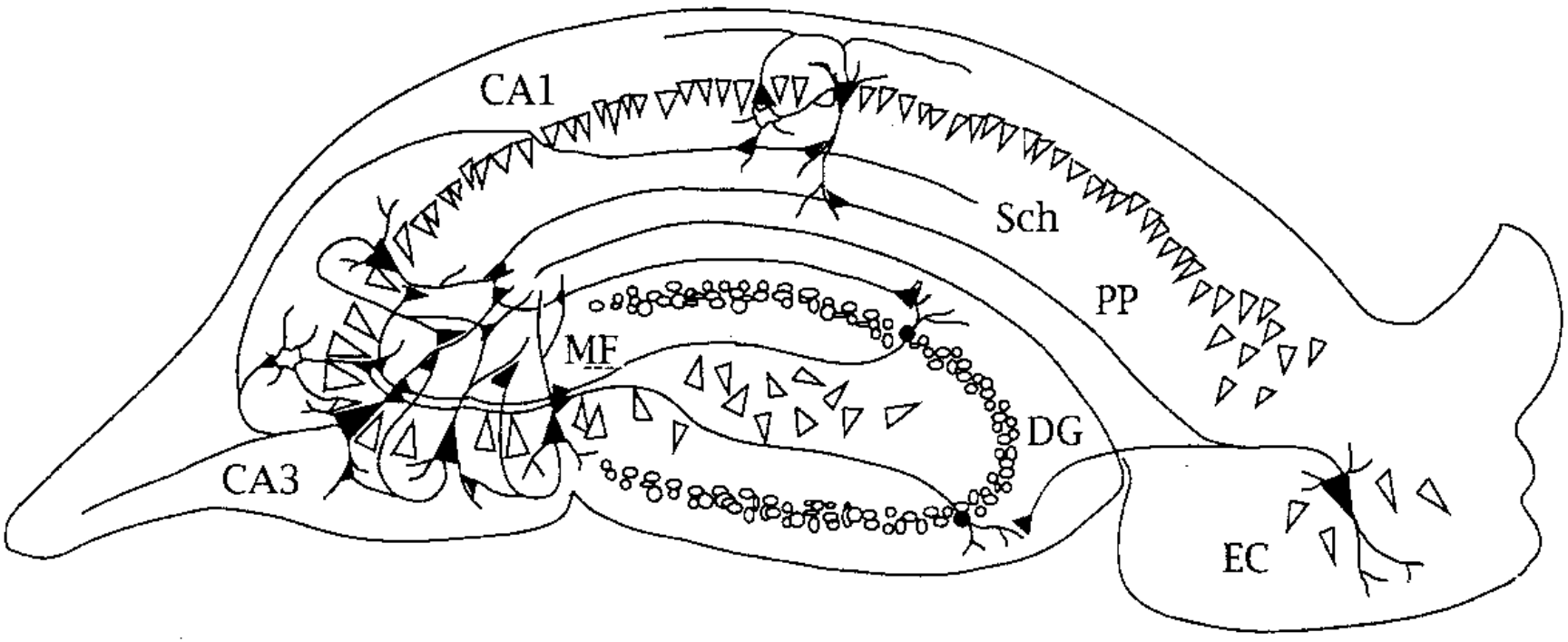
Deng et al., 2019

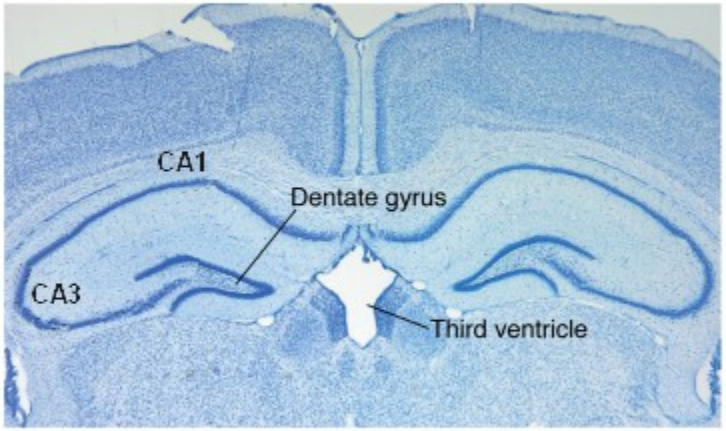
Hippocampus

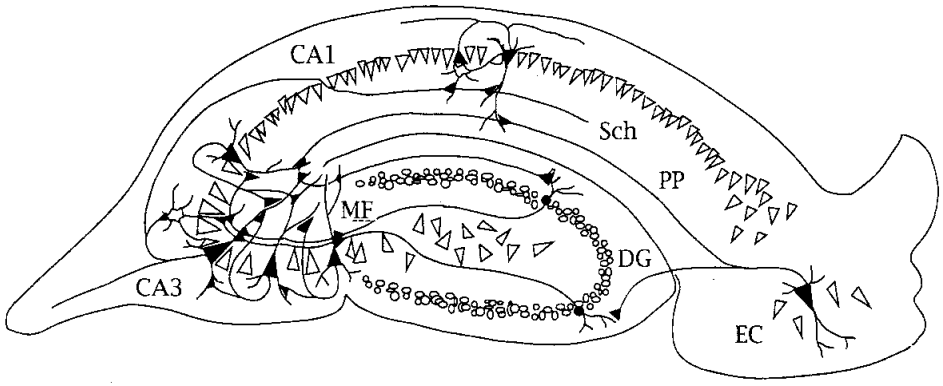




Hippocampus







Test

stimulation

Long-term potentiation

50 Hz

Stimulate presynaptic cell once

Same stimulus to presynaptic cell

Long-term depression

1 Hz

Stimulate presynaptic cell once

Same stimulus to presynaptic cell

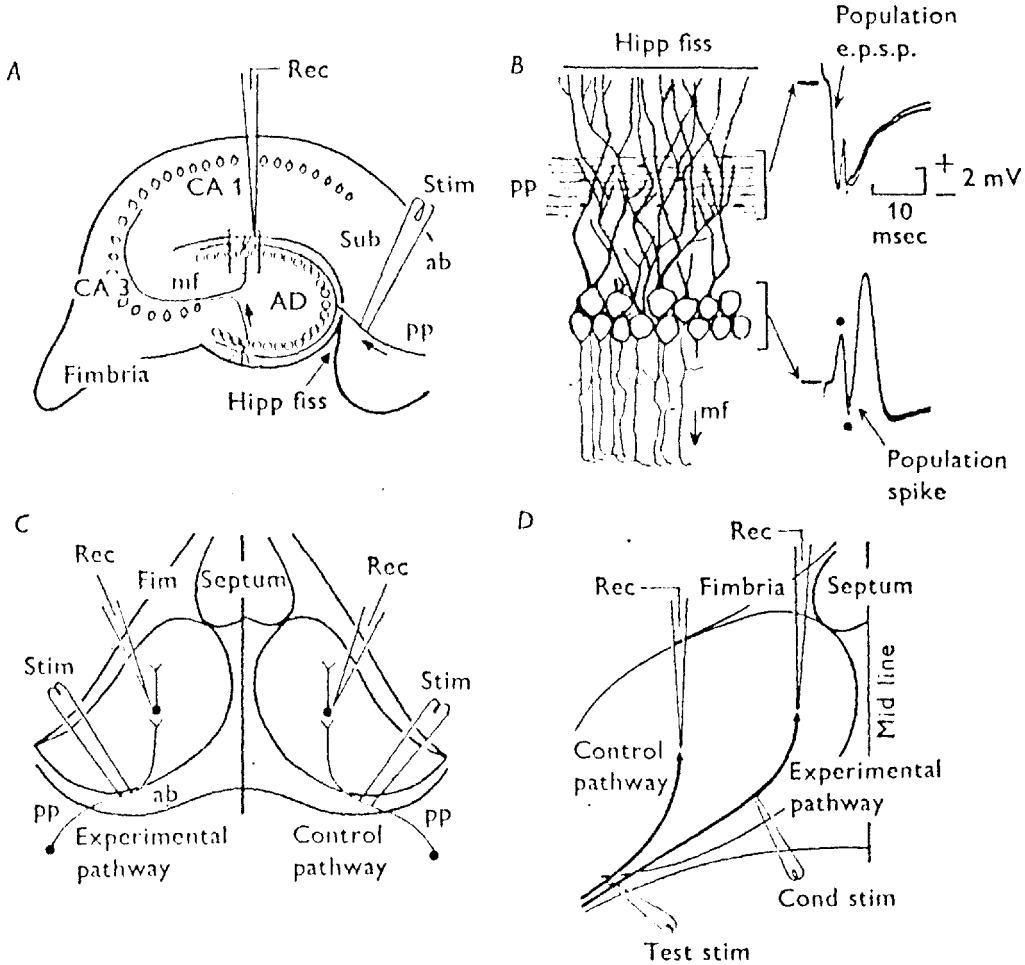
J. Physiol. (1973), **232**, *pp.* 331–356
With 12 text-figures
Printed in Great Britain

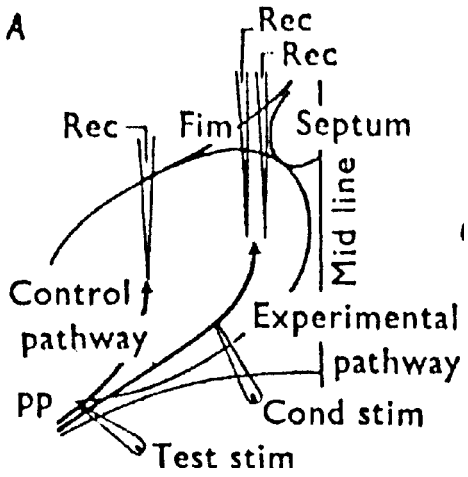
LONG-LASTING POTENTIATION OF SYNAPTIC TRANSMISSION IN THE DENTATE AREA OF THE ANAESTHETIZED RABBIT FOLLOWING STIMULATION OF THE PERFORANT PATH

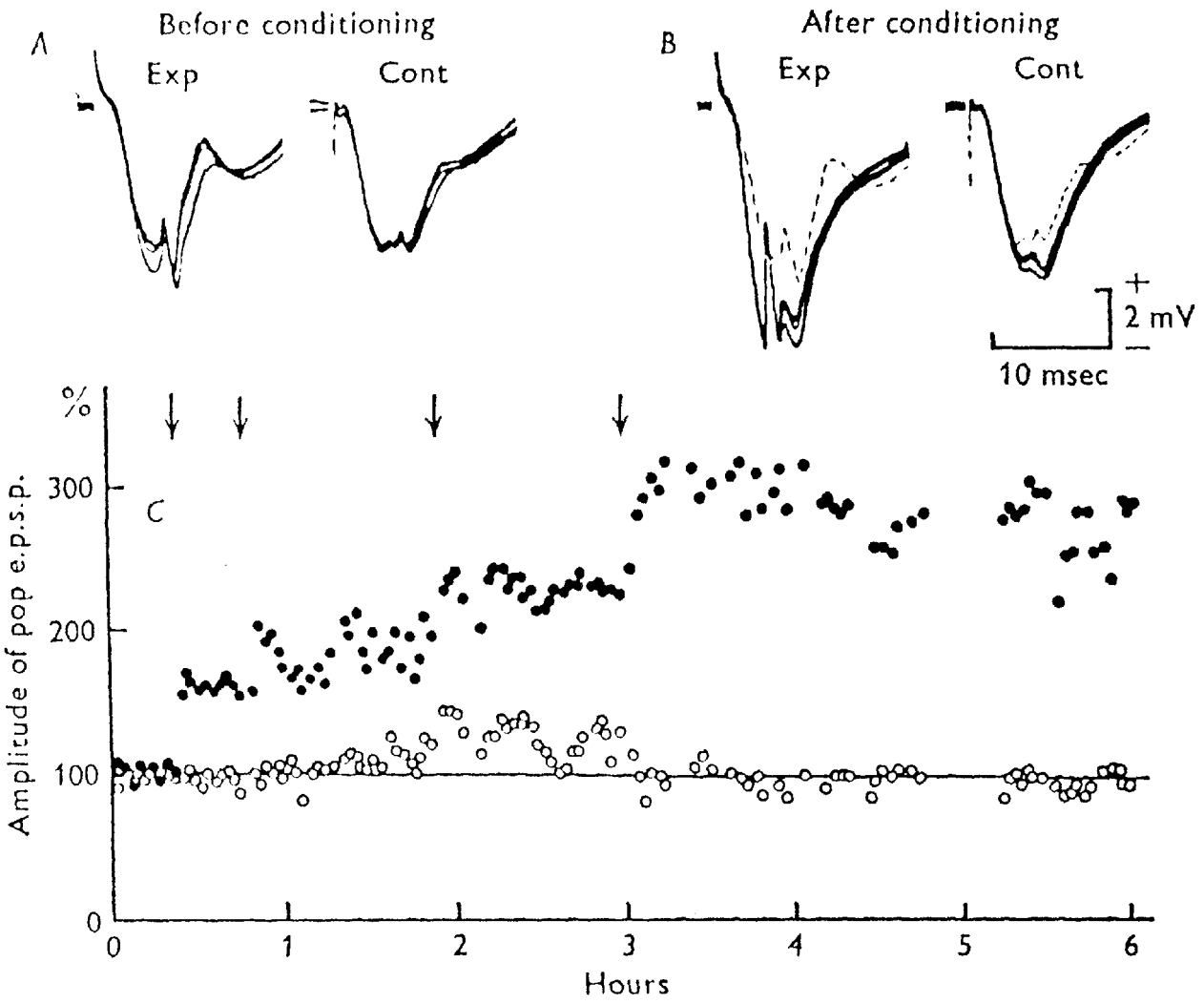
BY T. V. P. BLISS AND T. LØMO

From the National Institute for Medical Research, Mill Hill, London NW7 1AA and the Institute of Neurophysiology, University of Oslo, Norway

(*Received 12 February 1973*)




A
Rec
Rec
Rec
Fim
Septum
Mid line
Control
pathway
Experimental
pathway
PP
Cond stim
Test stim


A
Before conditioning
Exp
Cont
B
After conditioning
Exp
Cont
+
2 mV
10 msec
%
C
Amplitude of pop e.p.s.p.
300
200
100
0
0
1
2
3
4
5
6
Hours

Nature 305:719-21 1983

Intracellular injections of EGTA block induction of hippocampal long-term potentiation

Gary Lynch, John Larson, Stephen Kelso, German Barrionuevo & Frank Schottler

Center for the Neurobiology of Learning and Memory, University of California, Irvine, California 92717, USA

Hippocampal long-term potentiation (LTP) is a remarkably stable facilitation of synaptic responses resulting from very brief trains of high-frequency stimulation[1,2]. Because of its persistence and modest induction conditions, LTP represents a promising candidate for a substrate of memory. Some progress has been made in localizing the changes responsible for the effect; for example, it has been shown that LTP is not accompanied by changes in the fibre volleys of the test afferents[3] or by generalized alterations of the dendrites of their target cells[4]. However, it is unknown whether the potentiation is due to pre- or postsynaptic changes and there is evidence in favour of each (for example, see refs 5, 6). We now report that intracellular injections of the calcium chelator EGTA block the development of LTP. These results strongly suggest that LTP is caused by a modification of the postsynaptic neurone and that its induction depends on the level of free calcium.

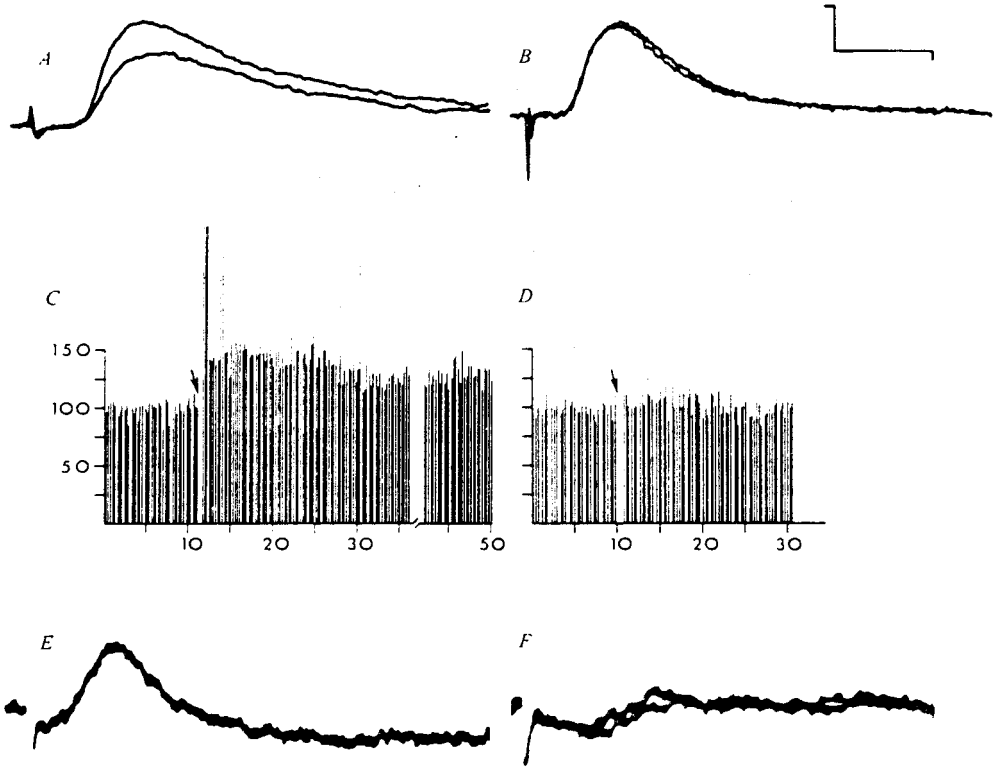


Table 1 e.p.s.p. amplitudes of cells which did not spike to single pulse stimulation after induction of extracellular long-term potentiation

	e.p.s.p. amplitude before high-frequency stimulation (mV)	Time (min) 5	10	15
Control	7.0 ± 0.6	+30 ± 5%	+30 ± 4%	+28 ± 4%
EGTA	7.1 ± 0.6	+8 ± 3%*	+1 ± 3%*	+5 ± 4%*

The e.p.s.p. amplitudes (mean ± s.e.m.) for 28 of 33 cells recorded with regular electrodes (control) and 24 of 26 cells recorded with EGTA-filled electrodes.

* $P < 0.001$.

Frequency-dependent involvement of NMDA receptors in the hippocampus: a novel synaptic mechanism

Caroline E. Herron, Robin A. J. Lester, Elizabeth J. Coan & Graham L. Collingridge

Department of Pharmacology, University of Bristol, Medical School, University Walk, Bristol BS8 1TD, UK

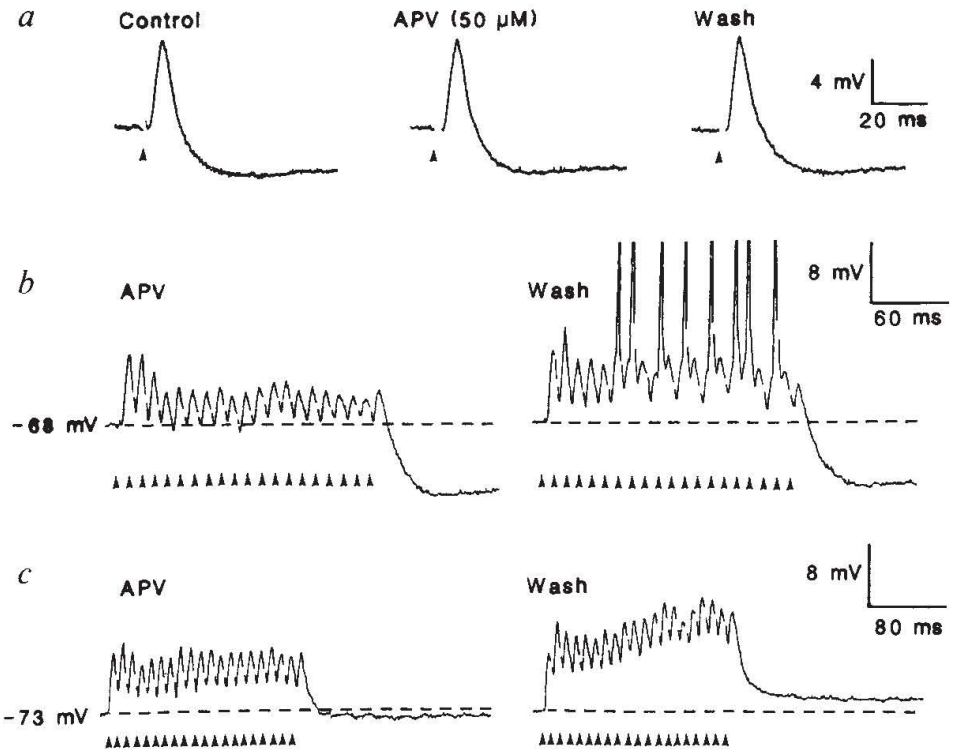
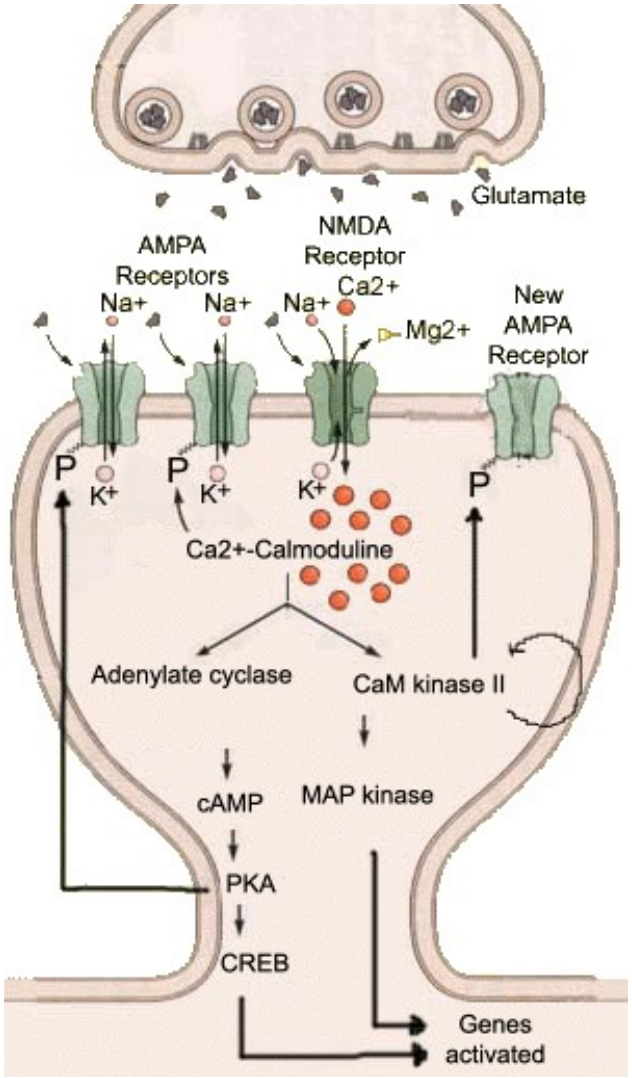


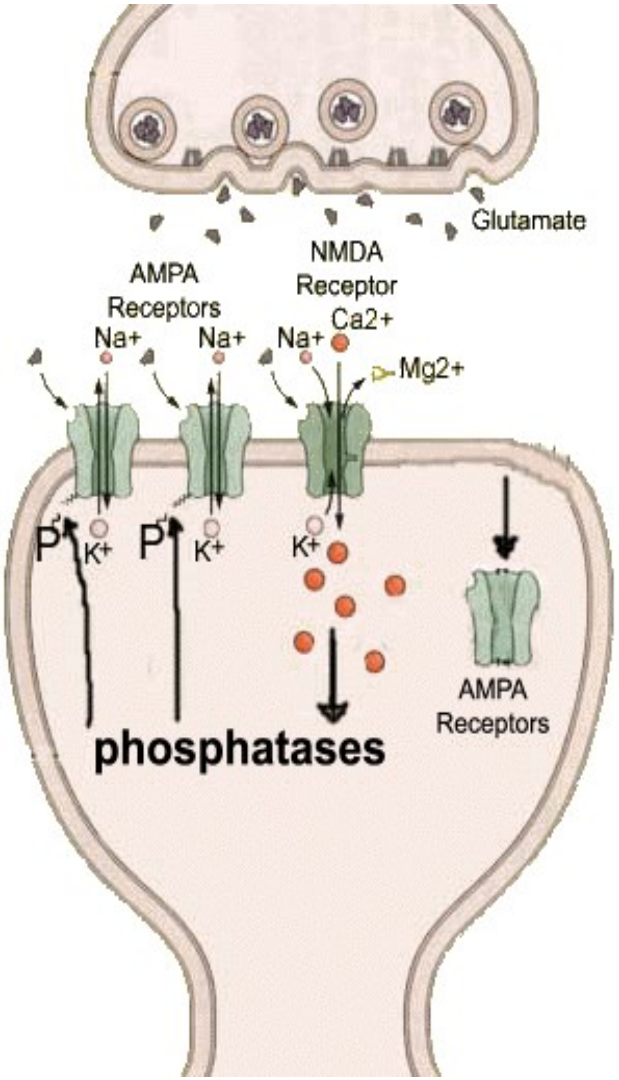
Fig. 2 Effect of 50 μM APV on synaptic responses recorded intracellularly in CA1 neurones in response to stimulation of the Schaffer collateral-commissural pathway. *a*, Averages of five successive records of synaptic potentials evoked at 30-s intervals before (control), during and after washout of APV. *b*, Single records of responses of the same cell to high-frequency stimulation (20 shocks at 10-ms intervals) in the presence and following washout of APV. The e.p.s.p.s shown in *a* (centre and right-hand records) were obtained immediately before the two respective periods of high-frequency stimulation. *c*, Single records of responses to high-frequency stimulation in another cell. The times of stimulation are indicated by arrowheads and stimulus artefacts have been blanked out for clarity. Stimulus intensity and membrane potentials were constant throughout. Action potentials in *b* are truncated.

Nature 322:265-268 1986

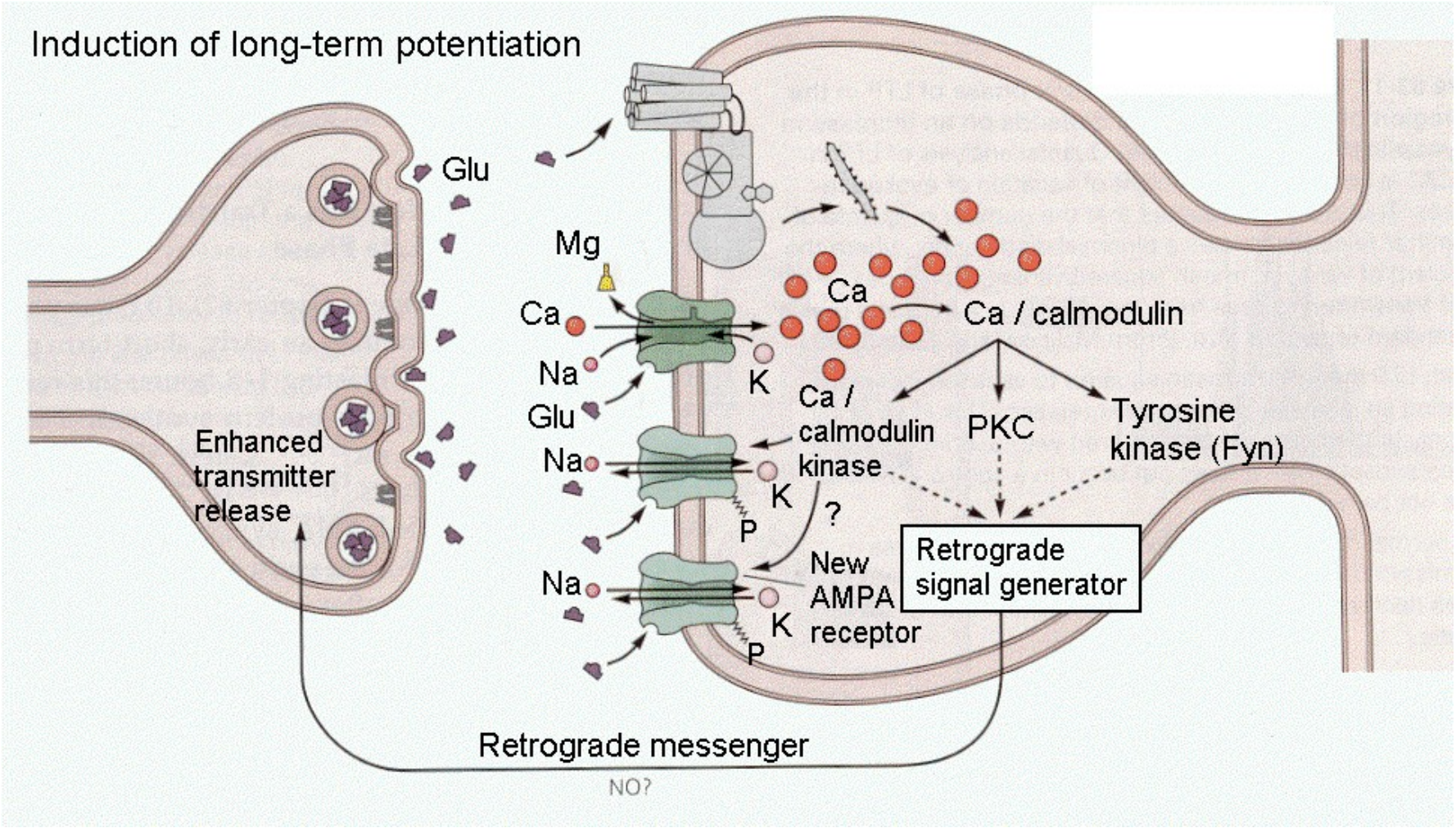
Long Term Potentiation



Long Term Depression

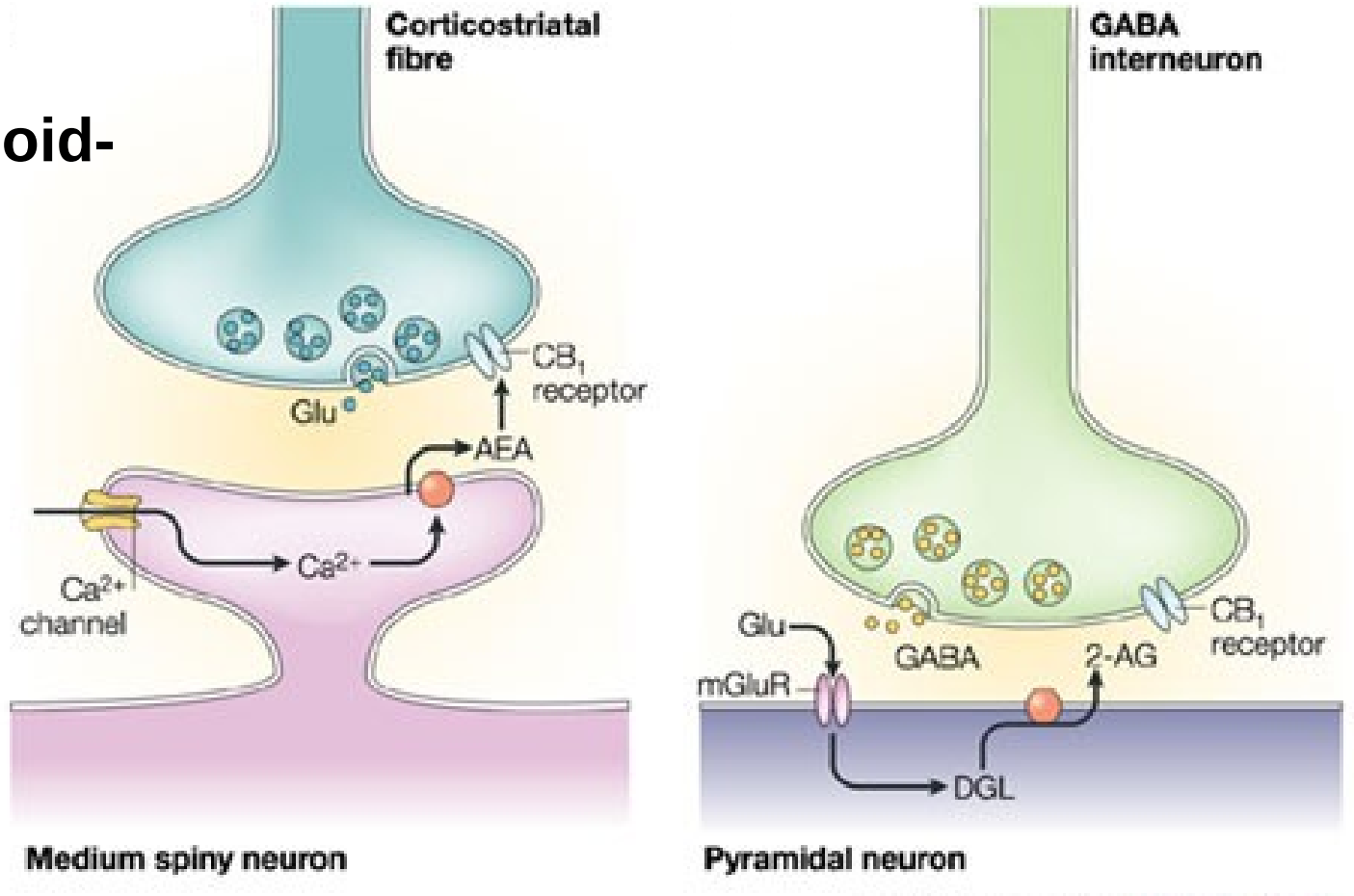


Long Term Potentiation, Cont'd



Long Term Depression, Cont'd

Endocannabinoid-mediated presynaptic inhibition



D. Piomelli 2003 Nature Reviews Neuroscience 4, 873-884

Long Term Potentiation, Cont'd