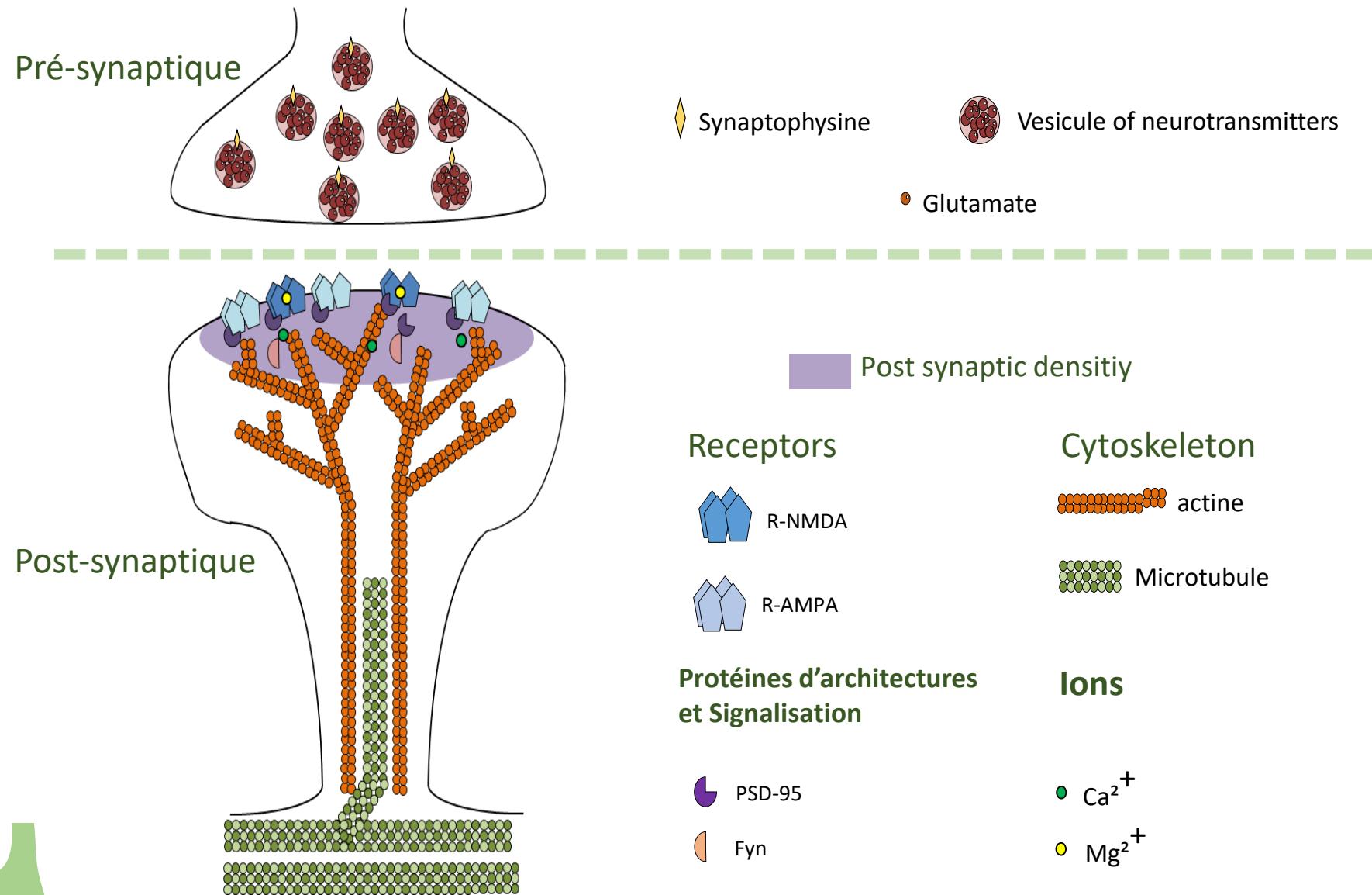


# **Mechanisms associated to the physiology of memory**

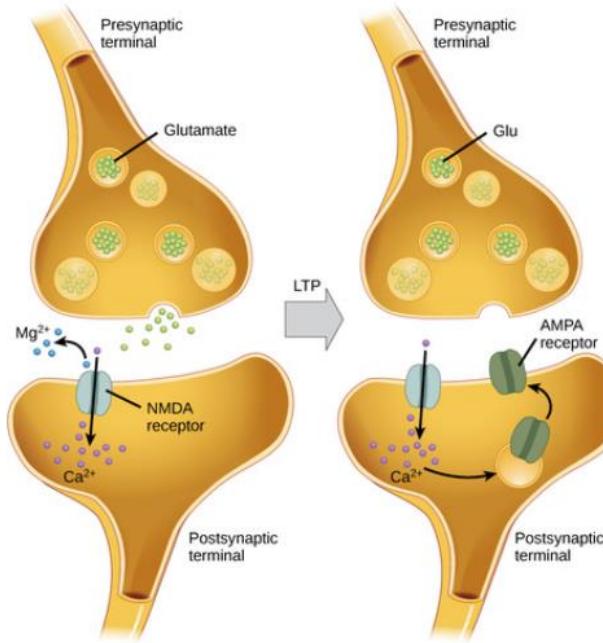
## **LTP and LTD**

# Excitatory synapses

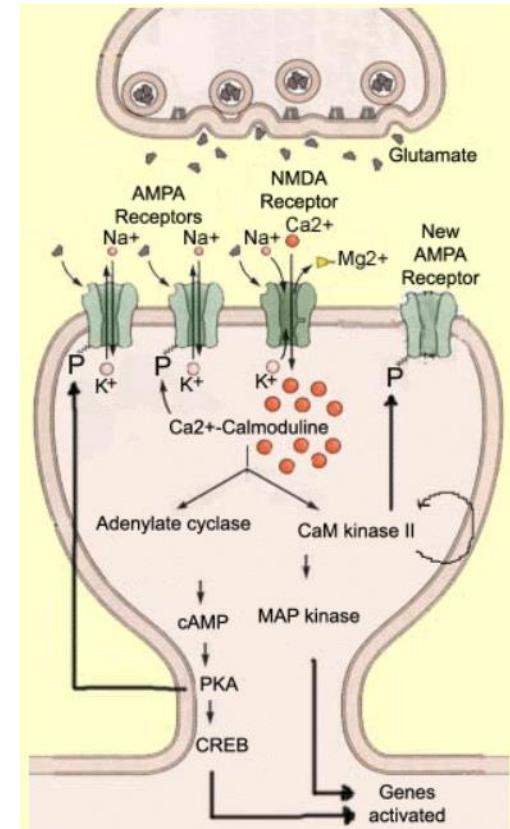


# MECHANISMS ASSOCIATED TO THE PHYSIOLOGY OF MEMORY

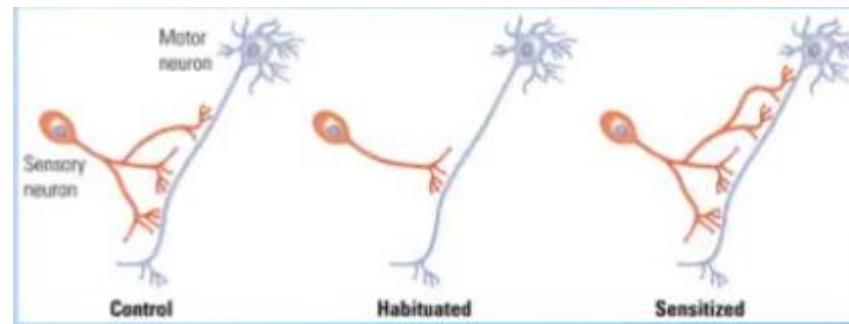
## Long term potentiation (LTP)



Early phase

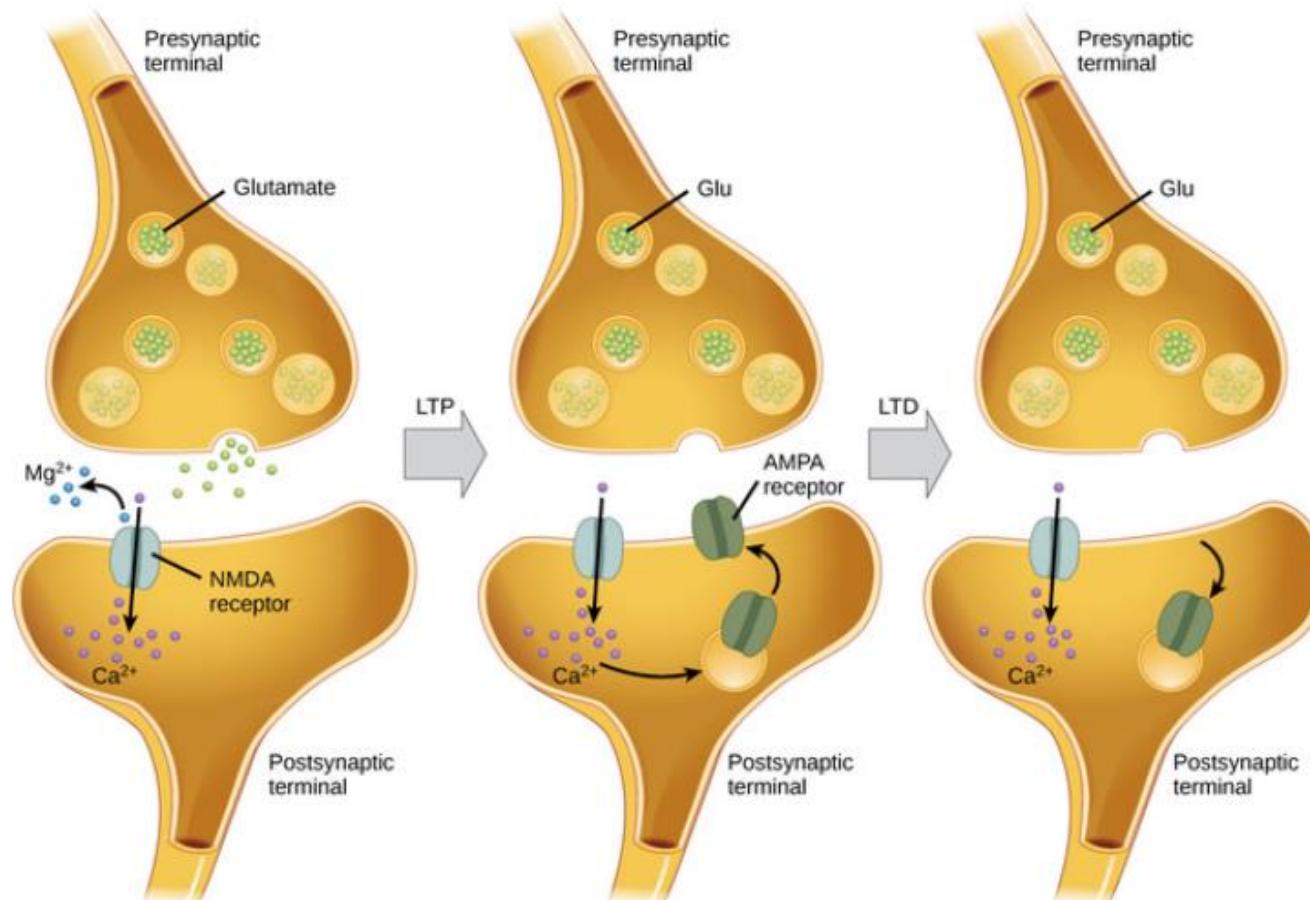


Late phase



# MECHANISMS ASSOCIATED TO THE PHYSIOLOGY OF MEMORY

## Long term depression (LTD)



The NMDA receptor is activated by glutamate binding, but only after depolarization removes inhibitory Mg<sup>2+</sup>. Once the Mg<sup>2+</sup> is removed, Ca<sup>2+</sup> can enter the cell.

Some AMPA receptors are present in the membrane initially. In response to an increase in intracellular Ca<sup>2+</sup>, more are inserted.

Low-frequency stimulation results in a different Ca<sup>2+</sup>-signaling cascade. AMPA receptor is removed from the membrane, and as a result, the nerve cell becomes less responsive to glutamate.

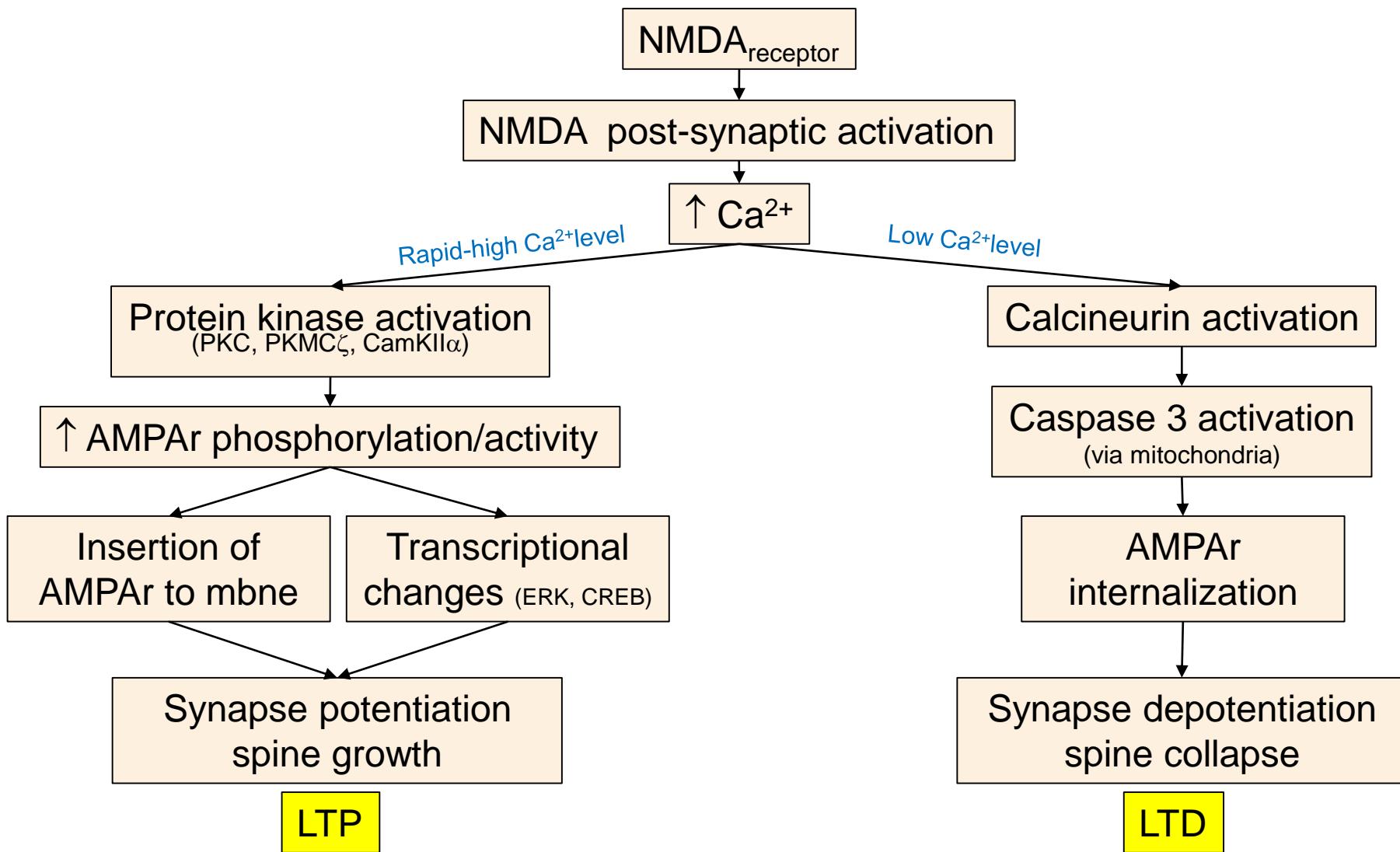
# MECHANISMS ASSOCIATED TO THE PHYSIOLOGY OF MEMORY

## Equilibrium between LTP and LTD

30–100 Hz

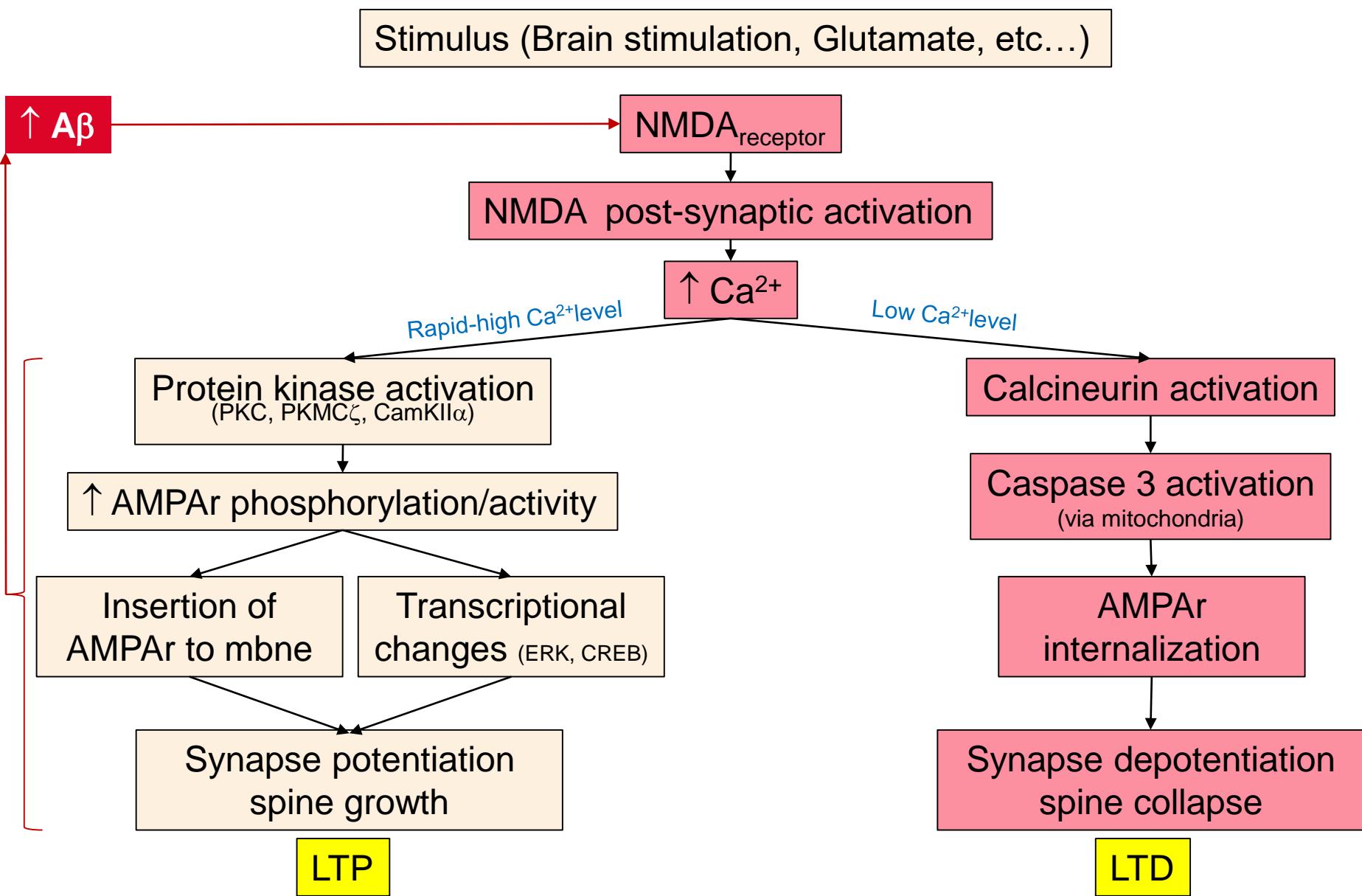
Stimulus (Brain stimulation, Glutamate, etc...)

1–3 Hz



# MECHANISMS ASSOCIATED TO THE PHYSIOLOGY OF MEMORY

## Equilibrium between LTP and LTD - Regulation by A $\beta$



# FACTORS SUGGESTING REGULATION OF LTP/LTD BY A $\beta$

- Neuronal activity increase A $\beta$  production
- A $\beta$  link to NMDAr
- A $\beta$  modulates intracell Ca<sup>2+</sup> (through many different mechanisms)

(Demuro et al., 2005; Hudry et al., 2012; Mattson et al., 1992; Wu et al., 2010; Zempel et al., 2010)

- A $\beta$  modulates calcineurin (Wu et al., 2012)
- A $\beta$  induces caspase-3 activation (Chen et al., 2013; D'Amelio et al., 2011; Liu et al., 2010)
- A $\beta$  causes internalization of AMPAr and NMDAr

(Hsieh et al., 2006; Koffie et al., 2011; Snyder et al., 2005; Wang et al., 2004)

Tau → regulates synaptic function

A $\beta$  → regulate the ability of Tau to regulate synaptic function

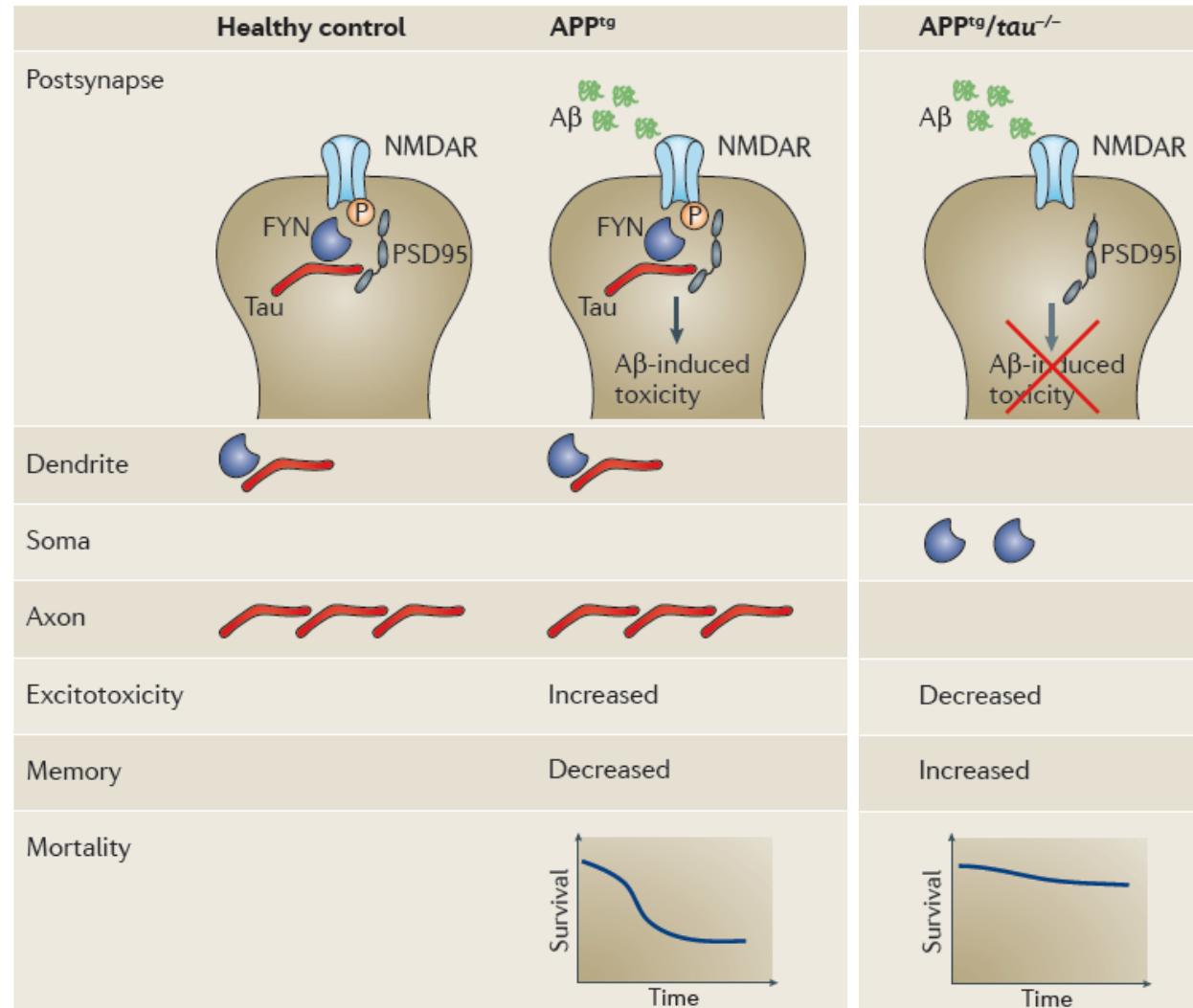
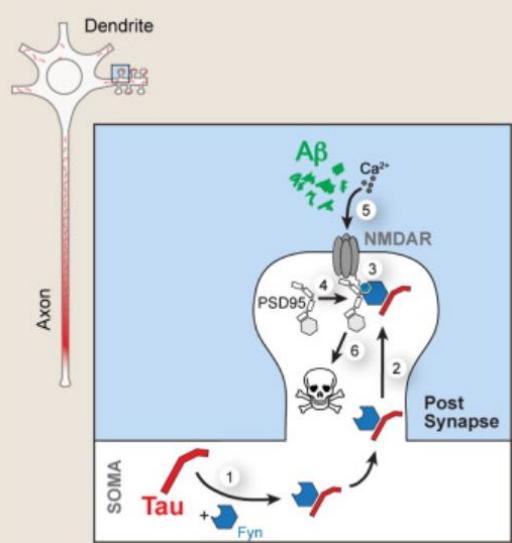
## General publications

(Christie et al., 2001; Li et al., 2009; Shankar et al., 2008)

# INTERACTION OF A $\beta$ AND TAU AT POST-SYNAPTIC LEVEL

## Interaction through the fyn/PSD95/NMDA<sub>r</sub>

Tau mediates  
A $\beta$  toxicity



Ittner, 2010. Cell 142(3), 387-397. DOI: 10.1016/j.cell.2010.06.036.

Ittner, L.M., Gotz, J., 2011. Nat. Rev. Neurosci. 12(2), 65-72. DOI: 10.1038/nrn2967.