I. Key Concepts

- · Major excitatory NT in brain: Glutamate
- Major inhibitory NT in brain: GABA
- Glutamate receptors have 2 large families:
 - Ligand-gated ion channels aka "ionotropic receptors"
 - G protein-coupled receptors called "metabotropic receptors"
- Ionotropic glutamate receptors divided into 3 classes which are named after the synthetic ligands that activate them;
 - o AMPA
 - o Kainate
 - o NMDA
- Individual excitatory synapses typically express several different subtypes of ionotropic glutamate receptors as well as metabotropic receptors
- NMDA receptors have 2 important biophysical properties (in contrast to AMPA and kainite):
 - o Highly permeable to Calcium
 - o Voltage dependent
 - ALLOWS CALCIUM ENTRY ONLY IF THE CELL IS DEPOLARIZED
- AMPA receptors mediate vast majority of excitatory synaptic transmission in brain
 - NM DA receptors play important role in triggering synaptic plasticity and, when over-activated, in triggering excite-toxicity
- 8 subtypes of metabotropic glutamate receptors
 - When localized to presynaptic terminal, they inhibit NT release
 - When localized to the postsynaptic membrane, they exert complex modulatory effects thru specific signal transduction cascades, which can lead to excitatory or inhibitory effects
- Most studied form of synaptic plasticity: Long-term potentiation (LTP) in hippocampus
 - Triggered by strong activation of NMDA receptors and the consequent large rise in postsynaptic Ca2+
 - There are several other types of LTP in the NS and are mediated via different mechanisms
- LTD = long-term depression
 - Long-lasting decrease in synaptic strength
 - Also occurs at most excitatory and some inhibitory synapses in brain
- · 2 major classes of GABA receptor

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