

Lecture 9 – Biochemistry of Synapses – D. Goldberg

I. Presynaptic

A. General Considerations

1. criteria for being transmitter
 - a. synthesized by cell
 - b. present at terminal and released in sufficient amounts
 - c. exogenous application mimics presynaptic stimulation
 - d. mechanism for removal from synaptic cleft
2. two types of transmitter
 - a. small molecule
 - i. synthesized at terminal and can be rapidly replenished
 - ii. rapid or modulatory postsynaptic effects
 - b. peptide
 - i. from precursor protein synthesized in cell body
 - ii. mainly modulatory postsynaptic effects

B. Small Molecules

see table

C. Peptides

1. cleavage from precursor allows amplification, multiple outcomes from single gene

D. Co-existence

1. small molecule and peptide transmitters present together in some terminals
2. unclear whether Dale's Principle that all terminals of a neuron release the same transmitter(s) is true

II. Postsynaptic

A. Receptors

1. ionophoric
 - a. rapid conformational change
 - b. mediates transmission
2. metabotropic (coupled to second messenger)
 - a. slower biochemical steps
 - b. modulates transmission
 - c. accesses second messenger via serpentine receptor which activates G protein
 - d. active G protein splits into subunits which affect enzymes or ion channels
 - e. 3 major second messenger pathways: cAMP (protein kinase A), IP_3 (Ca^{++})/diacylglycerol (PKC), arachidonic acid
 - f. reasons for using second messenger pathway
 - i. long-lasting effect
 - ii. signal amplification
 - iii. signal divergence from one receptor to multiple targets
 - iv. signal convergence from multiple receptors to one target
 - v. spread of signal through cell
 - vi. regulation of gene transcription

Relevant reading: chapters 13 and 15 in "Principles"